

In vivo Monitoring of Transcriptional Dynamics After Lower-Limb Muscle Injury Enables Quantitative Classification of Healing

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Supplementary Materials

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Text S2: Transcriptional Signatures Associated With Injured Muscle Tissue Extracellular Matrix

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Fig. S1. Immuno-histological analysis of muscle after cryo-injury.

Fig. S2. a) Example of reproducibility from RNA-Seq datasets. Biological replicates of *in vivo* isolated RNA samples from 24 hours after injury. Sequencing libraries were prepared from the isolated RNA and a strong correlation ($R^2 = 0.95$) was observed for two representative examples. b) Validation of RNA-Seq data with qPCR comparing the injured versus uninjured samples for the 3 hour time point. c) Validation of RNA-Seq data with qPCR comparing the injured versus uninjured samples for the 10 hour time point. d) Validation of RNA-Seq data with qPCR comparing the injured versus uninjured samples for the 24 hour time point.

Fig. S3. Number of differentially expressed genes.

Fig. S4. Gene Sets Activated Early After Injury (3-24 hrs) a) Enriched KEGG pathways from differentially expressed genes for the early time points (3-24 hrs). The size of the circle corresponds to the number of significant genes with each enriched pathway. b) Heatmap of genes associated metabolism expressed in the early time period. c) Gene expression profile of Arginase 1 (Arg1), which is a molecule emitted by type 2 macrophages to balance inflammatory reactive-oxygen species present in the injured tissue. Red-Injured, Blue-Uninjured

Fig. S5. Examples of alternative splicing in immune network of genes.

Fig. S6. Genes associated with hematopoietic activation, proliferation and anti-inflammatory cytokines activated in early & middle periods.

Fig. S7. Gene sets associated with extra-cellular matrix remodeling & satellite cell activation.

Fig. S8. a) Enriched KEGG pathways from differentially expressed genes for the late time points. The size of the circle corresponds to the number of significant genes with each enriched pathway. b) Heatmaps of gene sets activated in late period categorized by function.

Fig. S9. Area plots of FDR values for Gene Annotation (GO) clusters over time. GO terms were separated into major functional categories, and the IQR was computed for the terms in each group. The grey lines indicate the 25th and 75th percentiles, red lines denote the 25% of gene FDR values, the blue line denotes the median FDR value, and the green line denotes the 75% for FDR.

Fig. S10. Pathway-level scoring results for test datasets from PCA and the timepoint signatures methods. a). Principal component analysis. b) Normalized time point signatures method applied to mean pathway expression values. Timepoint signatures for 6 test samples and a truth training sample. The green curve indicates the control sample that was misclassified by the algorithm at the pathway level. Time point signatures for the 9 time points (blue lines) as well as 6 test samples (red and green lines).

Fig. S11. Differentially expressed gene pathways in injured samples over time.

Table S1. Significant GO clusters (FDR <0.05) identified for differentially expressed genes through the DAVID annotation tool. Each tab represents the annotations derived for each timepoint, clustered by function and sorted by FDR value from most to least significant.

Table S2: KEGG pathways identified for differentially expressed genes (FDR < 0.05). Pathways are listed for each timepoint and sorted by FDR value from most to least significant.

Table S3. Significant GO clusters identified from the 168h time point that were obtained from differentially expressed genes that were determined to contribute the largest variance at that time point.

Text S1: Transcriptional Signatures of Inflammation and Immune System Detected in Early Period

Pro-inflammatory cytokines and chemotactic protein members: IL-1 β , IL-6, IL-18, Tnf α , Osm, Ccl2, Ccr2, Cxcr2, Trem2, S100a8, FDR=2.21e-22 - GO:0034097, response to cytokine

Anti-inflammatory genes: Socs3, IL-1rn, IL-4ra, IL-10ra, IL-13ra1, FDR=4.31e-10 - GO:0050728, negative regulation of inflammatory response

Invading immune cell genes: Cd68, Ly6c, Cd14, Cd163, Mrc1, Ptprc, Cd24a, Cd63, Itgam, Clec7a, Ltf, Irf7, Hp, FDR=7.6e-7 - GO:0050900, leukocyte migration involved in inflammatory response

Cytokines and chemokines: Ym1, S100a9, Spp1, Ccr1, Ccl3, Ccl11, Lcn2, Cxcl5, Ccl12, FDR=3.8e-44 - GO:0001816, cytokine production, FDR=9.05e-14 - GO:0032602, chemokine production

Signaling lymphocytic activation molecule family: Slamf7, Slamf8, Ly9, FDR=3.44e-16 - GO:0046649, lymphocyte activation

Pro-apoptotic loci: Casp1, Casp4, Casp8, Apaf1, Fas, FDR=1.40e-9 - GO:2001235, positive regulation of apoptotic signaling pathway

Anti-apoptotic loci: Xiap, Birc3, Birc5, Api5, Bax, Mcl1, Bcl2l1, FDR=2.17e-23 - GO:0043066, negative regulation of apoptotic process

Text S2: Transcriptional Signatures Associated With Injured Muscle Tissue Extracellular Matrix

Structural components of extra-cellular matrix (ECM) remodeling: Col1a1, Col1a2, Col3a1, Col5a1, Col5a2, Col5a3, Col6a1, Col6a2, Col6a3, Eln, FDR=4.19e-111 - GO:0016043, cellular component organization

Connective tissue: Fbn1, Ctgf, Has1, Hbegf, Fn1, Sparc, Tnc, FDR=6.65e-14 - GO:0061448, connective tissue development

ECM cross-linking enzymes: Lox, Loxl1, Loxl2, Plod3, Leprel2, P4hb

Small leucine-rich proteoglycans: Dcn, Bgn, Kera, Vcan, Lum, Ogn, FDR=3.69e-28 - GO:0036211, protein modification process

Adhesive glycoproteins: Pcolce, Itgbpb1, Lgals1, Dpt, Postn, Emilin2, Efemp2, Igfbp7, FDR=3.36e-16 - GO:0043062, extracellular structure organization

Tgf- β superfamily: Tgf- β i, Tgf- β r1, Tgf- β r2, Tgf- β 1

Formation and stabilization of blood vessels and arterial repair: Ang, Angpt2, Angptl1, Angptl4, Angptl7, Cthrc1, Aif1, FDR=3.12e-10 - GO:0001525, angiogenesis

Contractile fibers: ActB, Actg, Capg, Arpc3, Cofil1, Tln1, Tagln, Vcl, RhoA, FDR=7.8e-5 - GO:0030833, regulate actin filament polymerization, FDR=1.5e-3 - GO:0032273, positive regulation of protein polymerization

Integrin-associated genes: Itga5, Itga7, Itgam, Itgav, Itgb1, Itgb2, FDR=3.34e-5 - GO:0007229, integrin-mediated signaling pathway

Mmps, Adams and Timps: Mmp2, Mmp3, Mmp8, Mmp14, Mmp19, Adam8, Adam15, Adam19, Timp1, Timp2, FDR=6.83e-8 - GO:0048771, tissue remodeling

Text S3: Injured Muscle Tissue Changes from Pro- to Anti-Inflammatory States Several Days After Injury

Innate immunity and microbial recognition: Tlr1, Tlr7, Tlr8, FDR=0.003 - GO:0034121, regulation of toll-like receptor signaling pathway

Antigen presentation and hematopoietic activation and proliferation: Ptprc, IL-21r, IL-17ra, Vav1, Lyz2, Csf1r, Csf2rb, Csf2ra, Il3ra, Il5ra, Ifi204, Aif1, FDR=1.4e-8 - GO:0042110, T cell activation, FDR=8.18e-19 - GO:0030097, Haematopoiesis

Anti-inflammatory cytokines: IL-1rl1, Il-4ra, IL-10ra, Msr1, IL-13ra1, S100a9, FDR=2.9e-10 - KEGG mmu04630, cytokine-cytokine receptor interaction, FDR=9e-3 - GO:0010934, macrophage cytokine production

Phagocytic and complement cascade genes: Cyba, Ncf1, Ncf2, Ncf4, C1qa, C1qb, C1qc, C1ra, C1s, FDR=3.37e-8 - GO:0006956, complement activation, FDR=7e-6 - GO:0006909, phagocytosis

Notch signaling: Dll1, Notch2, Myc, Rbpj, Cdkn1a, FDR = 3.69e-18, GO:0002684, positive regulation of immune system process

Bone morphogenetic proteins: Bmp1, Bmp4, FDR = 0.08, GO:0005125, cytokine activity

Actively proliferating cells: Cdk1, FDR = 9.63e-9, GO:0007049, cell cycle

Text S4: Activation of Muscle Repair Machinery

Satellite cell markers: CD34, Itga7, Itgb1, Sdc3, Sdc4, Sdcbp, Cav1, Cxcr4, Cdh15, Ly6a, FDR=4.933e-5 - GO:0007519, muscle tissue development

Muscle-fusion genes: Tmem8c, Cdh15, Capn2, Capns1, Myof, Cav3, Itgb1, Vcam1, Itga4, FDR=2.5e-6 - GO:0098602, single organism cell adhesion

Basement membrane genes: Col4a1, Col4a2, Dysf, Trim72, Lamc2, Cav3, Ahnak, Anxa1, Anxa2, Anxa5, FDR=4.78e-9 - GO:0061024, membrane organization

Muscle-specific actins, myosins, troponins, and tropomyosins: Actl9, Clrn1, Myh3, Myl4, Myl6b, Cald1, Tpm4, Tnni1, Tnni3, Tnnt1, Tnnt2, Tnncl, Tpm3, Des, Vim

Transcription factors: Itgb2, Rrad, Fos, JunB, FosB, Pbx2, Pbx3, Dusp5, MyC, BMyc, Mt3, Egr1, Egr2, Sgms2, Runx1, Grn, Pdlim3, Csrp3, Usf1, Arid5b, Naca, Ankrd1, Ankrd2, Atf3, Atf4, Atf6, Xbp1, Tead4, Nfe2l2, FDR=2.46e-10 - GO:0006351, transcription, DNA-templated

Text S5: Late Transcriptional Programs Activated in Response to Traumatic LLM

Chemotaxis genes: Ccl6, Ccl8, Ccl9, Cxcl16, Fcer1g, Fcgr3, FDR=1.9e-5

Mast cell activation: Fyb, Fcer1g, Fcgr3, Fcgr2b, Lat2, Lcp2, FDR=3.33e-5 - GO:0045576, mast cell activation

Fc receptors: Fcer1g, Fcgr1, Fcgr3, Fcgr2b, Clec7a, Colec12, Hck, Sirpa, Slc11a1, Vav1, FDR=0.035 for KEGG mmu04664, Fc epsilon RI signaling pathway.

Lectins: Clec12a, Clec4a1, Clec4a2, Clec4a3, Clec4n, Clec7a, Clec10a.

Collagen fibril organization: Adamts14, Col3a1, Col5a1, Col5a2, Dpt, Lox, and Anxa2, FDR = 1e-7)

ECM receptors: VLA proteins (α 2, α 5, α 8, α 9, α 10, α 11), cytoadhesins (β 3, A11- β), and proteoglycans (Cd44, Sdc3, Sv2), KEGG ECM-receptor interaction pathway, FDR = 5.7e-7

Angiogenesis genes: Col4a1, Col4a2, Robo4, Vash1, Sema5a, Sox18, GO:0001525, FDR = 3.24e-14

Muscle contraction and muscle system processes: Cacna1s, Myom1, Myh2, Myh4, Myh7, Nos1, Kcnma1, Ryr1, Trim63, FDR=6.7e-4 and 1.6e-3, respectively.

Ossification regulation: Gpnmb, Bglap, Sparc, Spp1, Runx2, Bmp1, Bmp5, Smad1

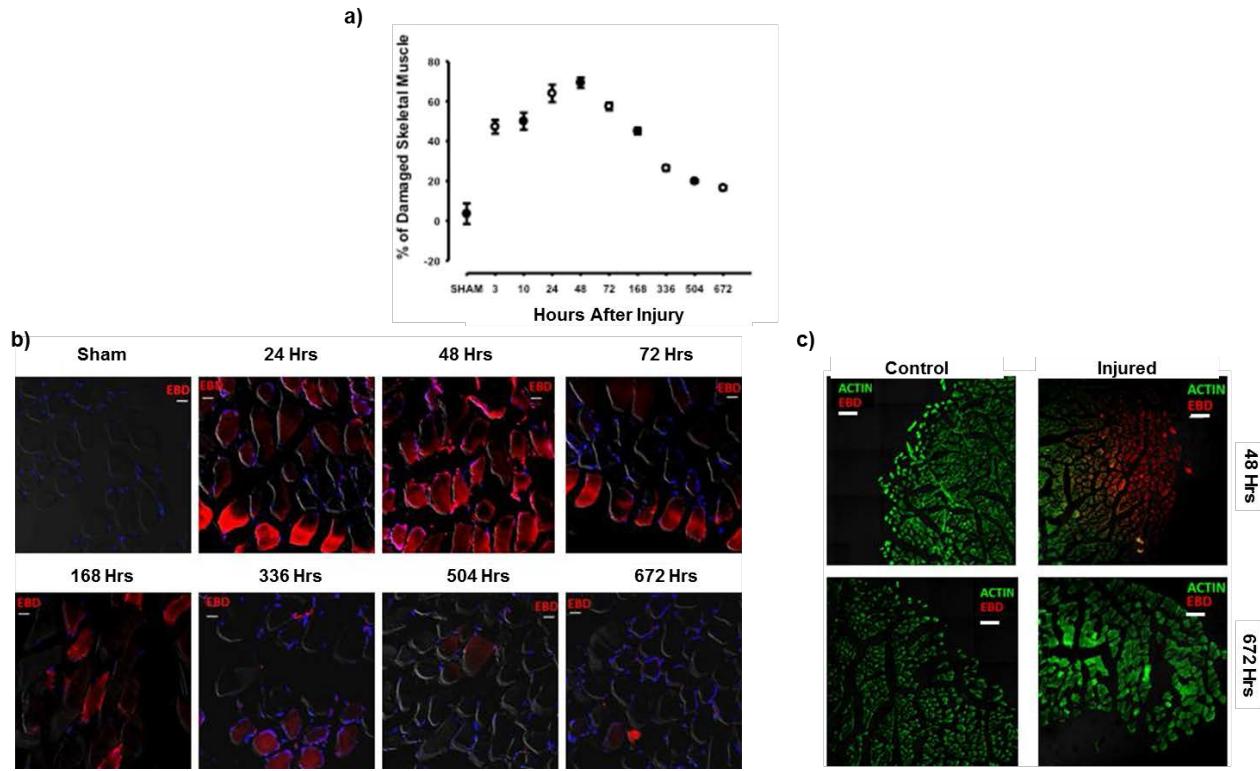


Fig. S1. Immuno-histological analysis of muscle after cryo-injury. a) Quantitative analysis of immuno-histological images revealed a gradual increase in tissue damage until 48 hours, indicating secondary damage to the muscle tissue occurred after the initial cryo-injury. b) Representative histological images of the injured TA stained with Evans Blue Dye (EBD – red) and DNA (blue) after several time points. c) Representative immuno-histological images at 48 hours and 672 hours after injury, whereby the green is stained for actin and red is stained for evans blue dye.

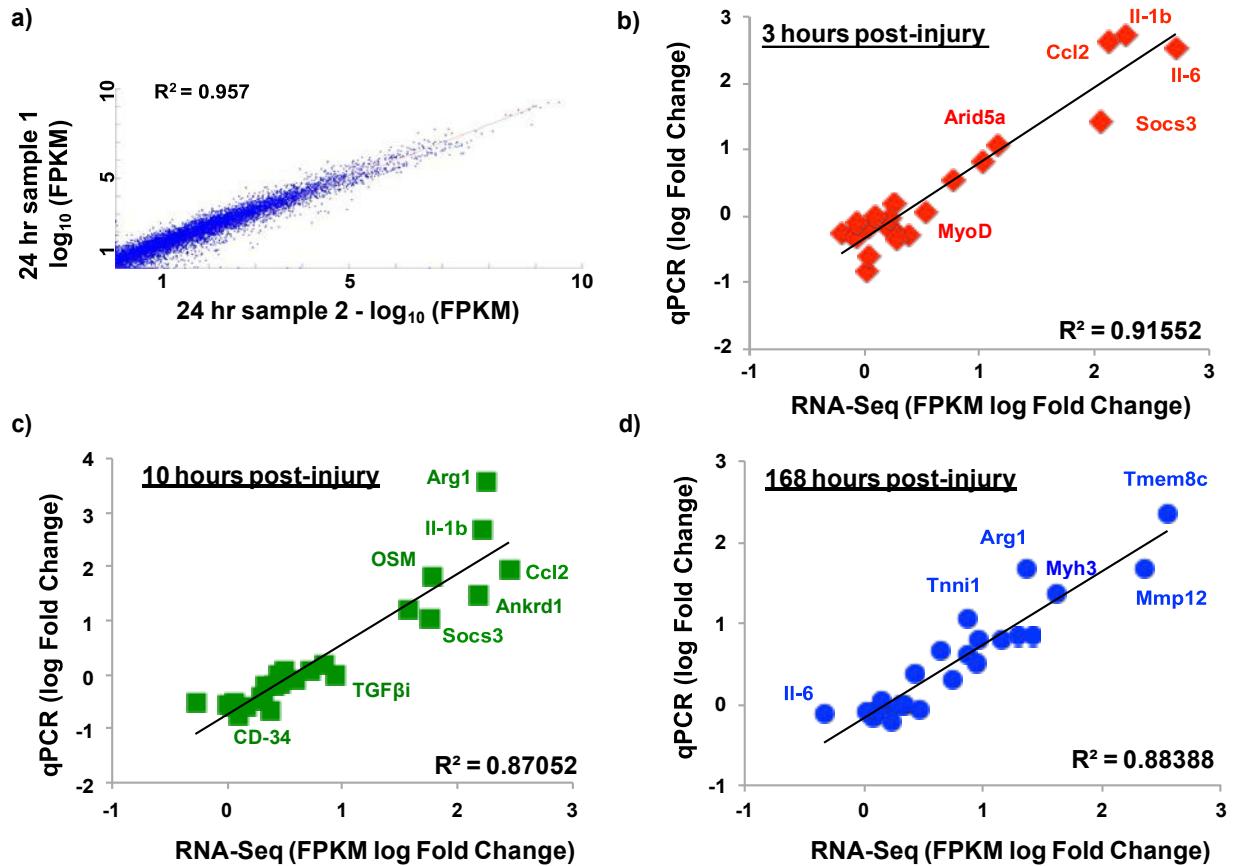


Fig. S2. a) Example of reproducibility from RNA-Seq datasets. Biological replicates of *in vivo* isolated RNA samples from 24 hours after injury. Sequencing libraries were prepared from the isolated RNA and a strong correlation ($R^2 = 0.95$) was observed for two representative examples. b) Validation of RNA-Seq data with qPCR comparing the injured versus uninjured samples for the 3 hour time point. c) Validation of RNA-Seq data with qPCR comparing the injured versus uninjured samples for the 10 hour time point. d) Validation of RNA-Seq data with qPCR comparing the injured versus uninjured samples for the 168 hr time point.

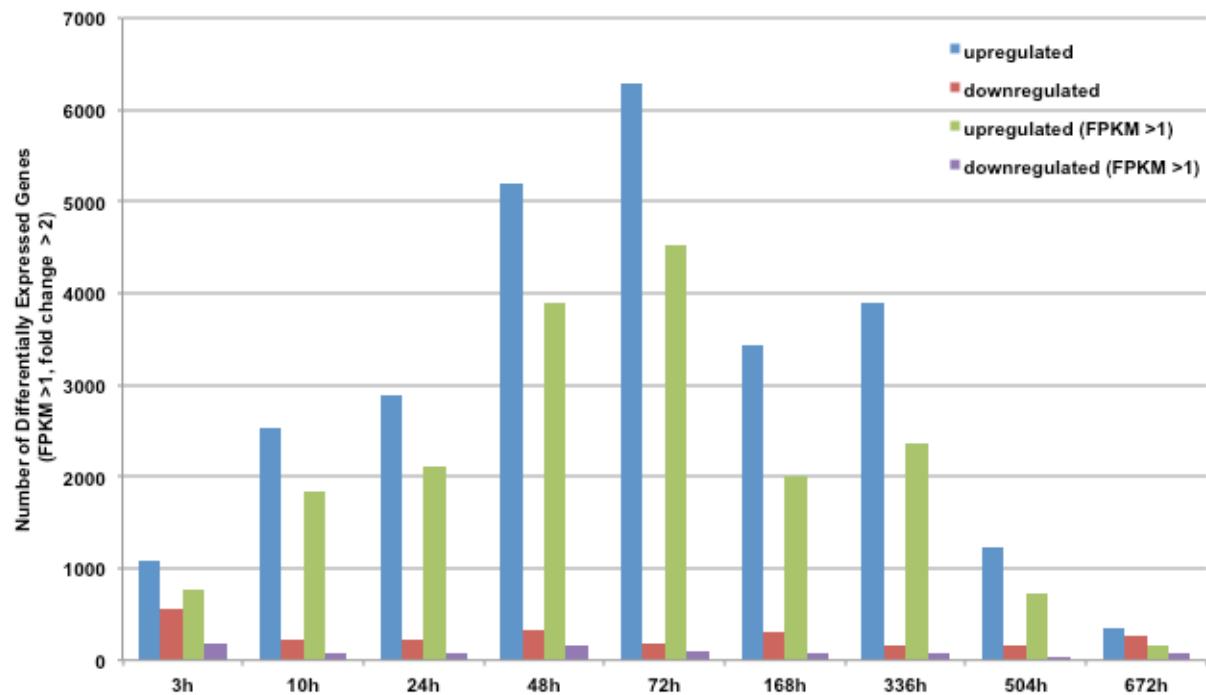


Fig. S3. Number of differentially expressed genes

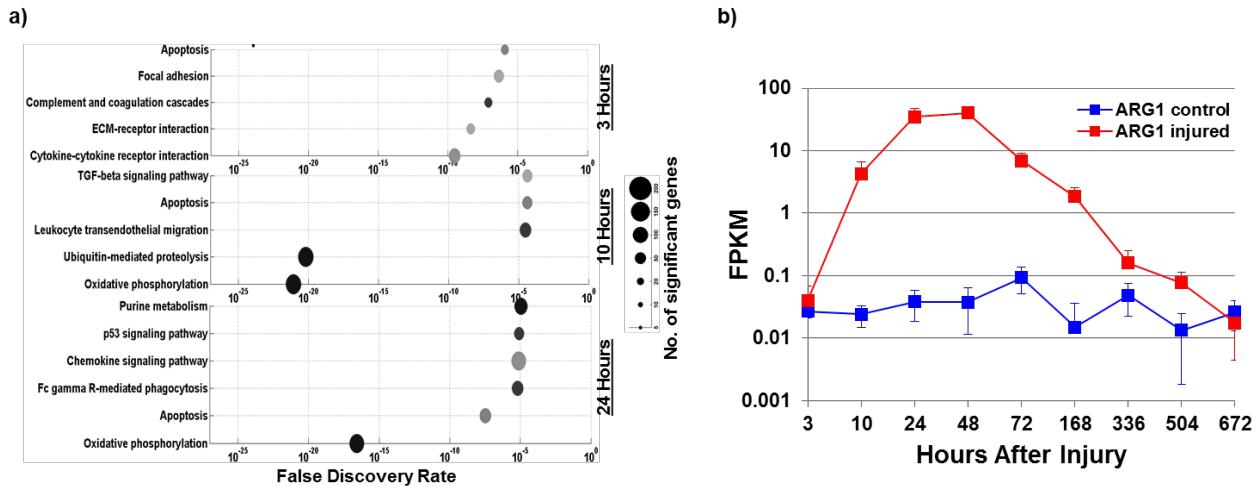


Fig. S4. Gene Sets Activated Early After Injury (3-24 hrs) a) Enriched KEGG pathways from differentially expressed genes for the early time points (3-24 hrs). The size of the circle corresponds to the number of significant genes with each enriched pathway. b) Heatmap of genes associated with metabolism expressed in the early time period. c) Gene expression profile of Arginase 1 (Arg1), which is a molecule emitted by type 2 macrophages to balance inflammatory reactive-oxygen species present in the injured tissue. Red-Injured, Blue-Uninjured.

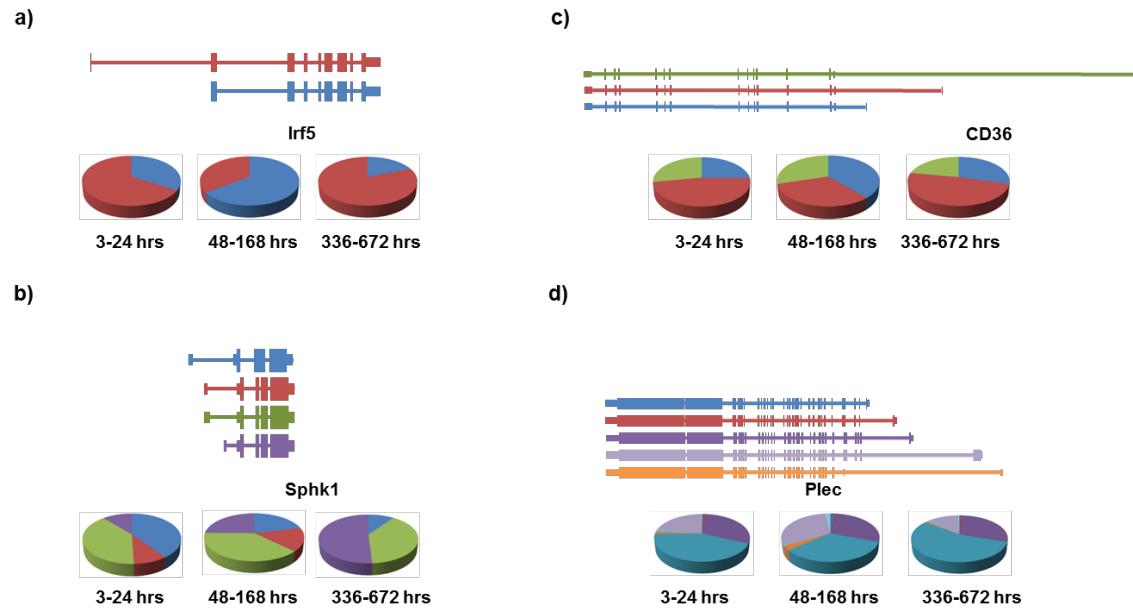


Fig. S5. Examples of alternative splicing in immune network of genes as determined by Cufflinks.

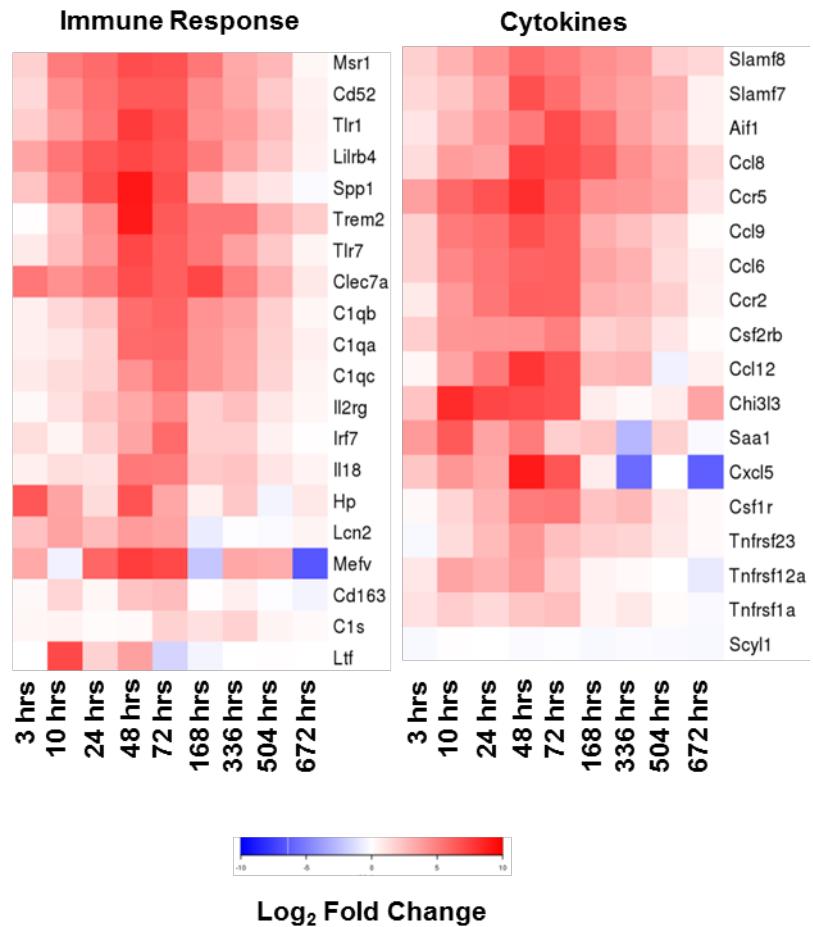


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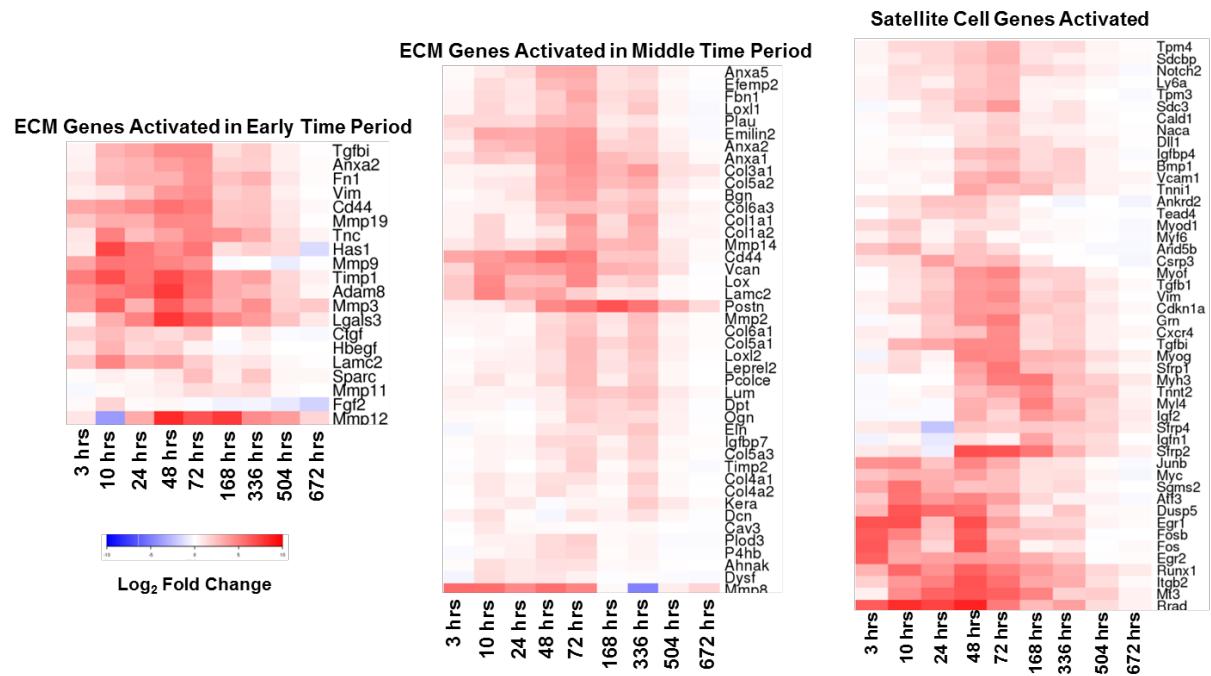


Fig. S7. Gene sets associated with extra-cellular matrix remodeling & satellite cell activation

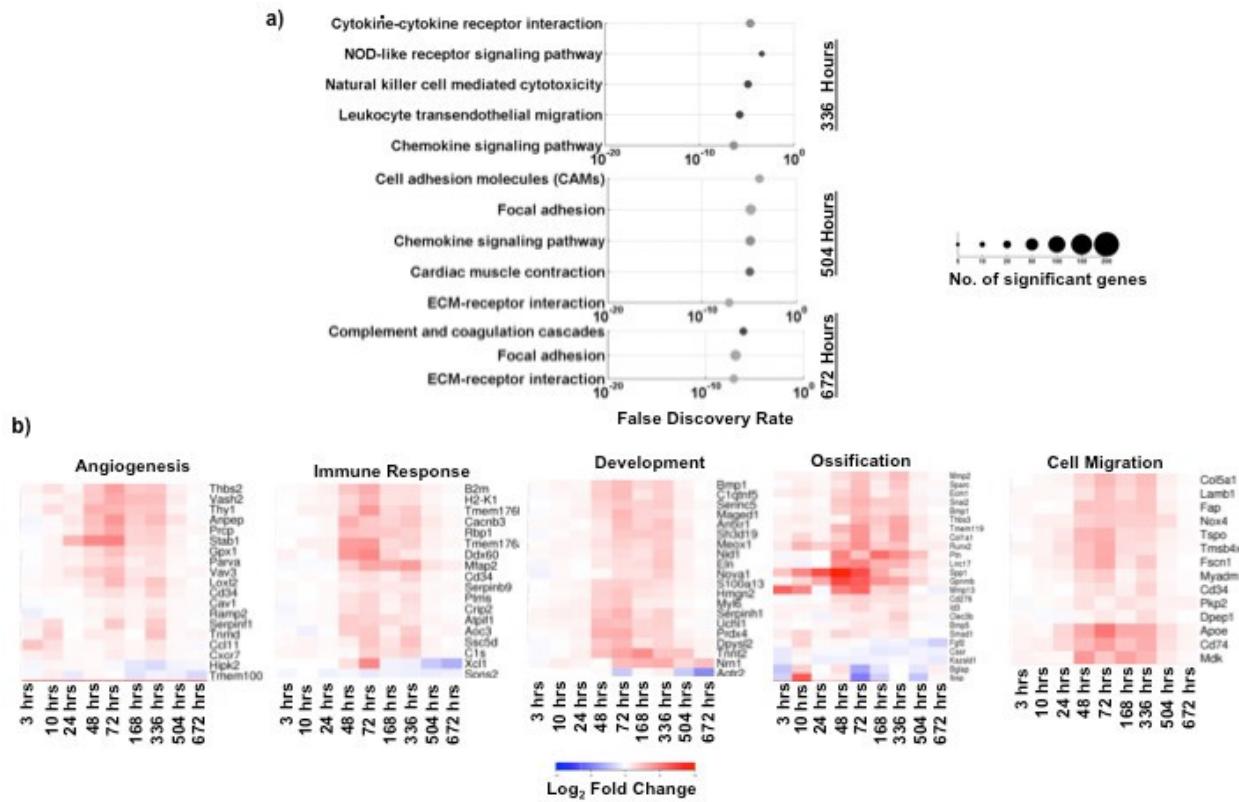


Fig. S8. a) Enriched KEGG pathways from differentially expressed genes for the late time points. The size of the circle corresponds to the number of significant genes with each enriched pathway. b) Heatmaps of gene sets activated in late period categorized by function.

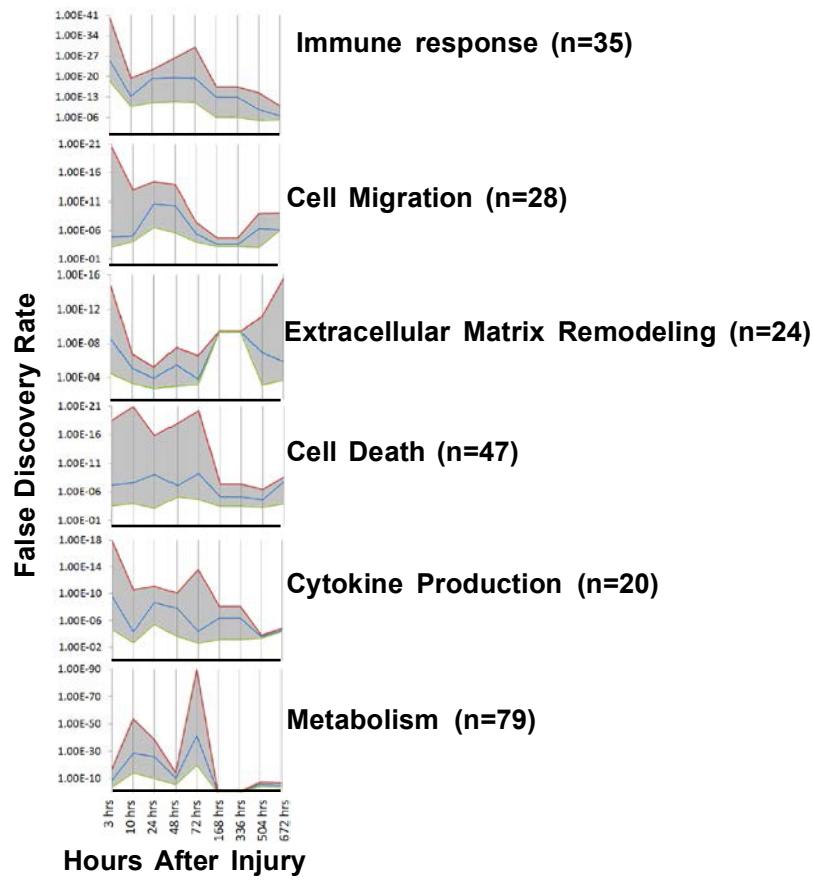


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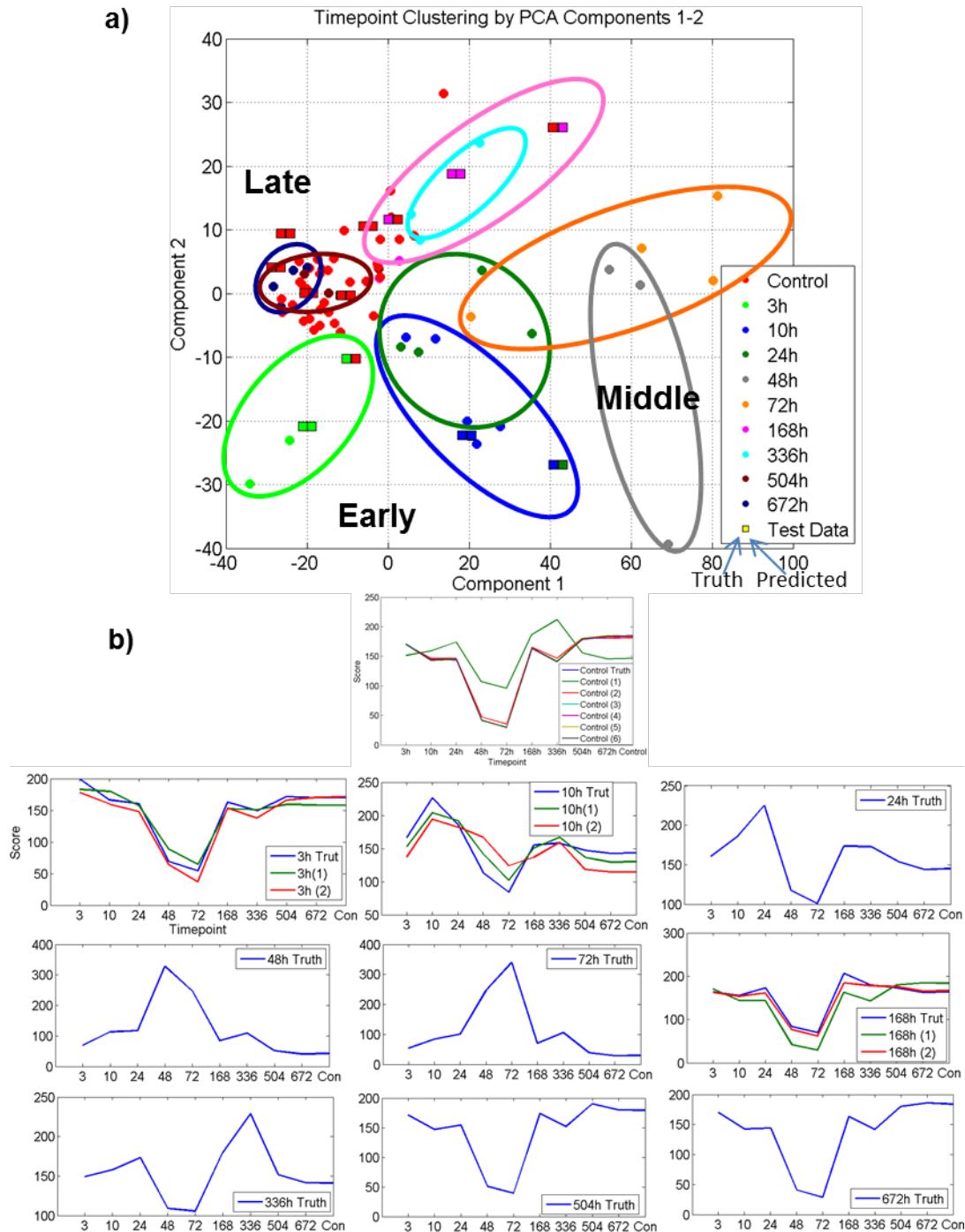


Fig. S10. Pathway-level scoring results for test datasets from PCA and the timepoint signatures methods. a) Principal component analysis. b) Normalized time point signatures method applied to mean pathway expression values. The top panel represents the timepoint signatures obtained for the uninjured control datasets for 6 test samples and a truth training sample. The green curve indicates the control sample that was misclassified by the algorithm at the pathway level. The next panels are derived from time point signatures for the 9 time points (blue lines) as well as 6 test samples (red and green lines).

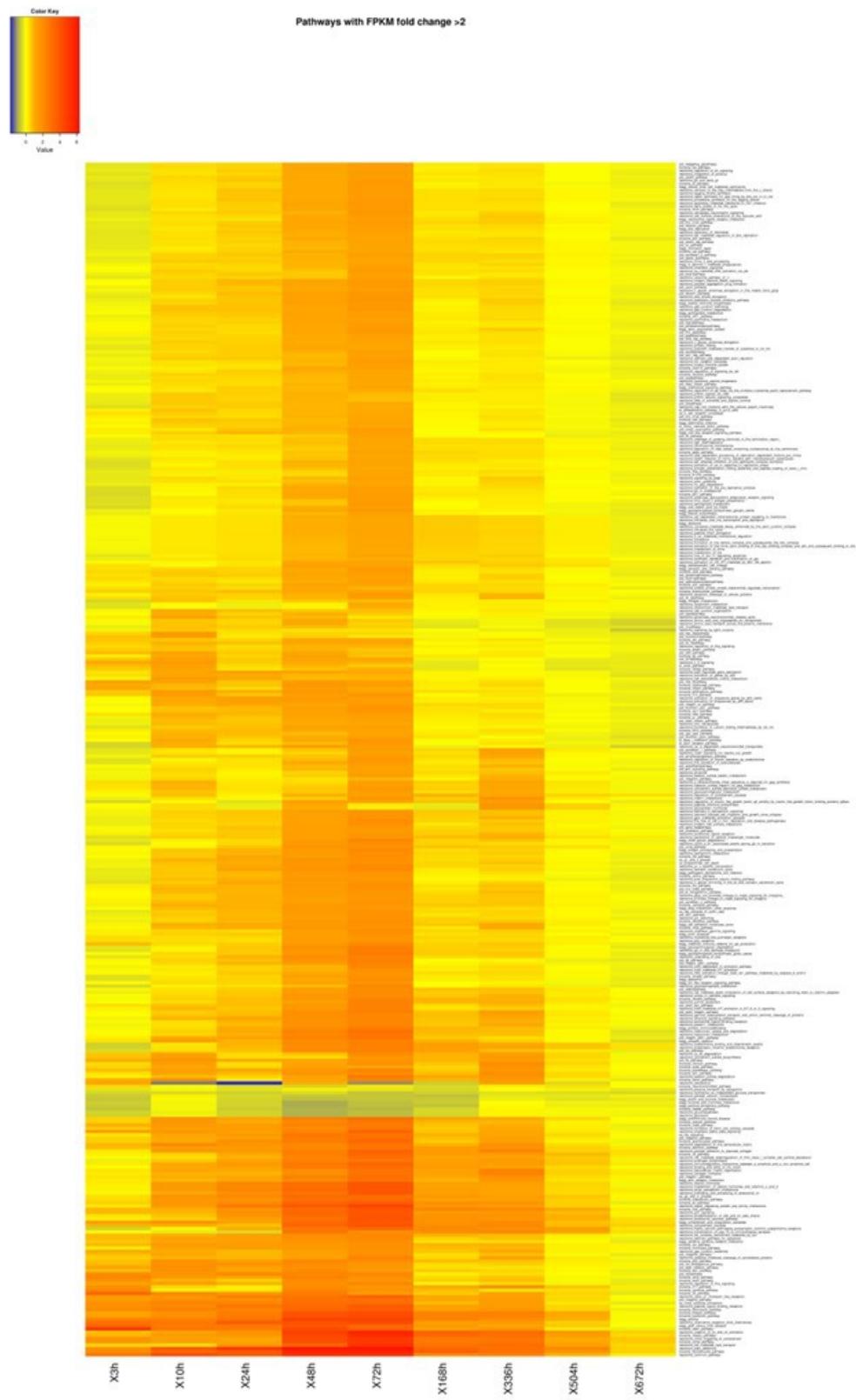


Fig. S11. Differentially expressed gene pathways in injured samples over time.

Table S1.A GO Terms upregulated 3 hours post injury

Table S1.B GO Terms upregulated 10 hours post injur

GOTERM_BP_FAT	GO:0051173 ⁺ positive regulation of nitrogen compound metabolic process	121	4.22	2.33E-06	PTPRC, IL6, CEBPB, CXBP1, AFF1, STAT3, IFR, IFR1, TXNL1, RBM14, RBM15, NFA, ARAP1	2080	526	13588	1.50	9.57E-03	2.67E-04	4.34E-03
GOTERM_BP_FAT	GO:0045944 ⁺ positive regulation of transcription from RNA polymerase II promoter	89	3.10	2.36E-06	PTPRC, IL6, CEBPB, CXBP1, AFF1, STAT3, IFR, IFR1, TXNL1, RBM14, RBM15, NFA, ARAP1	2080	358	13588	1.62	9.72E-03	2.64E-04	4.41E-03
GOTERM_BP_FAT	GO:0045941 ⁺ positive regulation of transcription	111	3.87	2.96E-06	PTPRC, IL6, CEBPB, CXBP1, AFF1, STAT3, IFR, IFR1, TXNL1, RBM14, RBM15, NFA, ARAP1	2080	475	13588	1.53	1.21E-02	2.98E-04	5.52E-03
GOTERM_BP_FAT	GO:0011628 ⁺ positive regulation of gene expression	113	3.94	3.77E-06	PTPRC, IL6, CEBPB, CXBP1, AFF1, STAT3, IFR, IFR1, TXNL1, RBM14, RBM15, NFA, ARAP1	2080	488	13588	1.51	1.54E-02	3.38E-04	7.02E-03
GOTERM_BP_FAT	GO:0006357 ⁺ regulation of transcription from RNA polymerase II promoter	136	4.74	5.27E-06	PTPRC, IL6, CEBPB, CXBP1, AFF1, STAT3, IFR, IFR1, TXNL1, RBM14, RBM15, NFA, ARAP1	2080	616	13588	1.44	2.15E-02	4.10E-04	9.82E-03
GOTERM_BP_FAT	GO:004595 ⁺ positive regulation of nucleobase, nucleoside, nucleotide and nucleic acid metabolic proc	116	4.04	6.74E-06	PTPRC, IL6, CEBPB, CXBP1, AFF1, STAT3, IFR, IFR1, TXNL1, RBM14, RBM15, NFA, ARAP1	2080	510	13588	1.49	2.74E-02	5.06E-04	1.26E-02
GOTERM_BP_FAT	GO:004595 ⁺ positive regulation of nucleobase, nucleoside, nucleotide and nucleic acid metabolic proc	119	4.15	9.65E-06	TBX1, AFF1, STAT3, GCK, IRS2, PFK1, RBM14, RBM15, NFA, ARAP1	2080	530	13588	1.47	3.91E-02	6.87E-04	1.80E-02

Table S1.C GO Terms upregulated 24 hours post injury

GOTERM_MF_FAT	GO:0005096-GTPase activator activity	56	1.96	3.05E-07	3H18P1, ARAP1, IQGAP2, ARHGAP15, TBC1D19, IQGAP1, TBC1D16, MMHA1, ARHGAP22, ARHGAP20, RIN1, TIAM2, ARHGAP1, RANBP1, ARHGAP11A, ARHGAP9, BCR, ARHGAP28, SIPA1L2, THY1, ARHGAP25, ARHGAP30, ACAP1, RIN1, RIN3, ARFGAP2, ARHGDIG, ARFGAP3, RAP1GAP, TBC1D9, GPM3, SIPA1, MYO9B, FANCI, ARAP1, DOCK2, RGS12, GMIP, GPM3L, RASA3, ARHGDA, ARHGDI8, TBC1D2, TBC1D8, TBC1D10C, ARB, TBC1D10A, RGS18, RGS16, RACGAP1, RGS14, USPENL, ADAP2, RGS2, CHML, GRTP1,	1935	192	13288	2.00	4.32E-04	2.70E-05	5.03E-04
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GOTERM_MF_FAT	GO:0016791 [“] phosphatase activity	50	2.32	2.99E-05	PP1PS2K, PGAM1A, PTPN22, PGAM2, PPMSK1, NTSC, PTPLR, PPAP2C, PP2B, PPP1R3A, LPN2, PTPRO, LPN3, PPMS1H, PPML1, PPML1M, PPFK8/3, NTSC5A, 963003320R0K, PPFK1, PPM1A, ACPS, PTPLB, PPFCB, PPFC3A, INPS95, PPCTC, PTPN7, PTPN6, PTTRC, PTTR6, PTN18, PTPN3, PTN4, PTTR4, EPMA2, EPH2, DUSP23, ATP1A1, BPGM, PTPN12, DUSP4, DUSP4, DUSP28, PTPA43, DUSP26, PTPN1, Annotation Cluster 19	Enrichment Score: 3.3671298805402657	50	PPHT1, DUSP8, DUSP6	1524	238	13288	1.83	3.77E-02	1.54E-03	4.88E-02													
Annotation Cluster 19	Term	Count	%	PValue	Genes				List Total	Pop Hits	Pop Total	Fold Enrichment	Benferroni	Benjamini	FDR													
GOTERM_BP_FAT	GO:0006631 [“] fatty acid metabolic process	48	2.23	1.46E-07	FADS1, PRKAQ2, L2C7A1, PPRA, AC0X1, AC0D85, ECH1, CP72, STAT5B, NDUFA1, EC0H3, CD74, MYOSA, PRKAG2, L2C7A1, PPRA, AC0X1, AC0D85, ECH1, CP72, STAT5B, NDUFA1, EC0H3, CD74, HADHA, HADHB, SCAMO1, FAR1, ELOVL2, PRKAQ2B, TNFRSF1A, AL0X5AP, PRKA2, ELOVL2, HADH, HPGDS, GHR, ACSL5, SCD1, CP71B, ACA2, SCDA2, ACADM, TXAS1, NCF1, AL0H5AL, ACADS, PDPN, GOTERM_BP_FAT	GO:0006631 [“] fatty acid metabolic process	48	FADS1, PRKAQ2, EPHM2, FA0DS3, CRAT, PHY, CPT1A, BRCAL, ACADVL, ALOX5, DEG51	1594	184	13588	2.22	5.31E-04	2.12E-05	2.68E-04													
Annotation Cluster 25	Term	Count	%	PValue	Genes				List Total	Pop Hits	Pop Total	Fold Enrichment	Benferroni	Benjamini	FDR													
GOTERM_BP_FAT	GO:0051110 [“] positive regulation of cellular component organization	32	1.49	2.08E-05	FMN1, PLKA, FGCR2B, TPPP, CFI1, CLECT7A	1594	122	13588	2.24	7.30E-02	1.26E-03	3.83E-02	Annotation Cluster 27	Term	Count	%	PValue	Genes				List Total	Pop Hits	Pop Total	Fold Enrichment	Benferroni	Benjamini	FDR
Annotation Cluster 27	Term	Count	%	PValue	Genes				1594	99	13588	2.50	2.12E-02	4.29E-04	1.08E-02													
GOTERM_BP_FAT	GO:0051493 [“] regulation of cytoskeleton organization	29	1.35	5.90E-06	CAPG, TMS94X, STMN1	1594	60	13588	2.98	3.09E-02	6.04E-04	1.59E-02	GOTERM_BP_FAT	GO:0032956 [“] regulation of actin cytoskeleton organization	21	8.63E-06	CORO1A, ARPC1A, ARPC2, CFI1, CAPB, RHOMA, SYNPO	1594	61	13588	2.93	4.08E-02	7.56E-04	2.10E-02				
GOTERM_BP_FAT	GO:0032970 [“] regulation of actin filament-based process	21	0.98	1.14E-05	CORO1A, ARPC1A, ARPC2, CFI1, CAPB, RHOMA, TMS94X, SYNPO	1594	154	13588	2.10	4.88E-02	8.77E-04	2.53E-02	Annotation Cluster 30	Term	Count	%	PValue	Genes				List Total	Pop Hits	Pop Total	Fold Enrichment	Benferroni	Benjamini	FDR
Annotation Cluster 30	Term	Count	%	PValue	Genes				1594	154	13588	2.10	4.88E-02	8.77E-04	2.53E-02													
GOTERM_BP_FAT	GO:0023043 [“] regulation of organelle organization	38	1.77	1.37E-05	MID1IP1, UBE2B5, FMN1, ARPC1B, CORO1A, PLK4, YWHN, MAD2L1, CFI1, CAPG, TMS94X, STMN1	1594	361	13588	1.69	1.45E-02	7.32E-04	1.86E-02	GOTERM_MF_FAT	GO:0030695 [“] GTPase regulator activity	70	3.25	1.14E-05	SH3BP1, ARAP1, BCAR3	1524	361	13288	1.69	1.45E-02	7.32E-04	1.86E-02			
GOTERM_MF_FAT	GO:0030695 [“] GTPase regulator activity	70	3.25	1.14E-05	SH3BP1, ARAP1, BCAR3	1524	361	13288	1.69	1.45E-02	7.32E-04	1.86E-02	Annotation Cluster 32	Term	Count	%	PValue	Genes				List Total	Pop Hits	Pop Total	Fold Enrichment	Benferroni	Benjamini	FDR
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GOTERM_BP_FAT	GO:0002684 [“] positive regulation of immune system process	50	2.32	8.11E-07	FCB, FGCR1, FGCR3, CORO1A, COKN1A, PLCG2, CLECTA, H2-DM4, SASH3	1594	206	13588	2.07	2.95E-03	8.94E-05	1.49E-03	Annotation Cluster 58	Term	Count	%	PValue	Genes				List Total	Pop Hits	Pop Total	Fold Enrichment	Benferroni	Benjamini	FDR
Annotation Cluster 58	Term	Count	%	PValue	Genes				1594	206	13588	2.07	2.95E-03	8.94E-05	1.49E-03													
GOTERM_BP_FAT	GO:0044271 [“] nitrogen compound biosynthetic process	61	2.84	2.55E-05	APRT, AMPD1, ADI1, P2XRA, ATP6V0E2, ADcy9, CLCTA2, SLC7A2, PTEN, PTTRC, CARD9, H2-M2L, IZF1, Annotation Cluster 69	GO:0044271 [“] nitrogen compound biosynthetic process	61	APRT, HPR7, ATP1B2, LDH1, PNP, ATPHFD1, ANKL, GOT1, HOC, IMPDH1, ATP8B4, HPMRMA1, FICM, ATPV1H, PADI2, PADI4, ATPVIA, NME1, ADK, RIM1, ATP5CK1, ADOL, RBT1, ALDH1A1, BCAT2, SRA, NAGS, ASXL1, A2H1, CMK1, ADA, TYMS, ATMS, HMAS, DCTD, TCRL1, CERPA, ODC1, ADSL1, NOS1, NIPR2, ATP1A1, ATP1A3, AMP02, AMP03, MMAB, ATP13AA, BCAT2, BCKDAH, ALDH5A1, BCKDK, BCAT2S, BCDDH, HBDAH, GHR, AUH	1594	302	13588	1.72	8.85E-02	1.47E-03	4.68E-02													
Annotation Cluster 69	Term	Count	%	PValue	Genes				List Total	Pop Hits	Pop Total	Fold Enrichment	Benferroni	Benjamini	FDR													
GOTERM_BP_FAT	GO:0009081 [“] branched chain family amino acid metabolic process	10	0.46	1.06E-05	BCAT3, BCKDAH, ALDH5A1, BCKDK, BCAT2S, BCDDH, HBDAH, GHR, AUH	1594	15	13588	5.68	3.77E-02	7.12E-04	1.94E-02																

Table S1.E GO Terms upregulated 72 hours post injury

GOTERM_BP_FAT	GO:0006793-phosphorus metabolic process	175	6.16	5.82E-06	CDK20, DUSP6	2002	866	13588	1.37	2.33E-02	2.36E-04	1.08E-02
Annotation Cluster 35												
Category	Term	Count	%	PValue	Genes	List Total	Pop Hits	Pop Total	Fold Enrichment	Benferroni	Benjamini	FDR
GOTERM_BP_FAT	GO:0033559-unsaturated fatty acid metabolic process	19	0.67	6.23E-07	FCER1A, TBKAS1, PTG52, NCF1, POPN, FASD1, EPHK2, LTC4S, CD74, GGT5, TNFRSF1A, PTG5, MAST2, CDK2, CDK5, PKCC, PRK, PRKCA, PRKCB, MAST3, OSM, ATM, CNTF, CNTF14, DUSP6, CDK2, CDK5, PKCC, PRK, PRKCA, PRKCB, MAST3, OSM, ATM, CNTF, CNTF14, PRK, NOUFB1, PRK, PRM1A, ATP9G1, ISCP10, GALR2, GALR1, STAT4, PRKB, PRKB2, BUB1, DCLX1, TES, TCRG1, PTPRC, ALPK1, PTTR, RLT, POK3, HCK, PTTR4, NOUFB1, AXL, ATP5F1, CDK9, GSG2, CDC25B, DUSP5, CCNB1, RPSKA6, DUSP4, RPSKA4A, GCK, PTPA43, RPSKA1, PYN, GYK, JAK3, DUSP9, CIT,	2002	36	13588	3.58	2.53E-03	0.035-05	1.16E-03
GOTERM_BP_FAT	GO:0006690-icosanoid metabolic process	17	0.60	7.22E-06	HPGD, RNPEP, HPGD5, MGST2	2002	34	13588	3.39	2.89E-02	2.76E-04	1.34E-02
Annotation Cluster 40												
Category	Term	Count	%	PValue	Genes	List Total	Pop Hits	Pop Total	Fold Enrichment	Benferroni	Benjamini	FDR
GOTERM_BP_FAT	GO:0005077-negative regulation of immune response	14	0.49	2.33E-05	SPN	2002	26	13588	3.65	9.02E-02	8.00E-04	4.33E-02
Annotation Cluster 43												
Category	Term	Count	%	PValue	Genes	List Total	Pop Hits	Pop Total	Fold Enrichment	Benferroni	Benjamini	FDR
GOTERM_BP_FAT	GO:0031341-regulation of cell killing	16	0.56	5.44E-06	KL81B, LAG3	2002	30	13588	3.62	2.19E-02	2.23E-04	1.01E-02
GOTERM_BP_FAT	GO:0001910-regulation of leukocyte mediated cytotoxicity	16	0.56	5.44E-06	KL81B, LAG3	2002	30	13588	3.62	2.19E-02	2.23E-04	1.01E-02
Annotation Cluster 44												
Category	Term	Count	%	PValue	Genes	List Total	Pop Hits	Pop Total	Fold Enrichment	Benferroni	Benjamini	FDR
GOTERM_BP_FAT	GO:0032101-regulation of response to external stimulus	33	1.16	1.87E-05	FCGR3, ANXA2, CD99B, FCGR2B, NPY, FABP7	2002	103	13588	2.17	7.33E-02	6.62E-04	3.49E-02
Annotation Cluster 50												
Category	Term	Count	%	PValue	Genes	List Total	Pop Hits	Pop Total	Fold Enrichment	Benferroni	Benjamini	FDR
GOTERM_BP_FAT	GO:0005077-monovalent inorganic cation transmembrane transporter activity	33	1.16	1.79E-07	SLC9A9, ATP5E, SLC36A1, COX7B, COX7C, ATP5G1, UQCRC1, COX5A, COX5B, UQCRC2, UQCRC1, COX6B1, ATP5L, ATP5D, COX6B2, ATP5D02, ATP5K, ATP5L, TCRG1, COX7A2, COX8B, SLC9A9, ATP5E, SLC36A1, COX7B, COX7C, ATP5G1, UQCRC1, COX5A, COX5B, UQCRC2, UQCRC1, COX6B1, ATP5L, ATP5D, COX6B2, ATP5D02, ATP5K, ATP5L, TCRG1, COX7A2, COX8B,	1916	87	13288	2.63	2.37E-04	1.97E-05	2.93E-04
GOTERM_MF_FAT	GO:00015078-hydrogen ion transmembrane transporter activity	31	1.09	4.92E-07	COX7A2, ATP5F1, COX6C, ATP5E4, UQCRC1, COX6A2, ATP5D2	1916	82	13288	2.62	6.51E-04	4.07E-05	8.05E-04

Table S1.F GO Terms upregulated 168 hours post injury

Table S1.G GO Terms upregulated 336 hours post injury

Table S1.H GO Terms upregulated 504 hours post inj

Table S1.I GO Terms upregulated 672 hours post inj

Table S2.A KEGG pathways significant at 3 hours

Category	Term	Count	%	PValue	Genes	List	Total	Pop	Hits	Pop	Total	Fold	Enrichment	Bonferroni	Benjamini	FDR
KEGG_PATHWAY	mmu04060:Cytokine-cytokine receptor interaction	49	4.52	2.96E-08	OSMR, CXCR2, IL17RA, TGFBR2, CXCR4, IL1RAP, CSF3R, CSF2RB, IL1B, FAS, IL13RA1, CSF2RA, EGFR, LTBR, INHBB, OSM, TNFRSF10B, PPBP, CCR2, PDGFRA, CXCL1, CSF1, IL1R2, CCL3, IL1R1, CCL2, CSF2RB2, TNFRSF12A, CSF1, CCR1, IL4RA, CXCL2, CXCL9, CCL9, PFA, CNTFR, CCL7, CCL6, CCL24, TNFRSF1A, TNFRSF1B, IL10RA, BMP2, TGFBR1, TGFBR2, CCL11, CXCL14,	434	244	5738	2.66	4.88E-08	4.88E-08	3.59E-07				
KEGG_PATHWAY	mmu04512:ECM-receptor interaction	25	2.31	4.36E-09	TNC, COL3A1, SDC4, SDC2, CD44, COMP, COL6A2, COL6A1, COL11A2, THBS1, THBS2, THBS3, THBS4, SPP1, FN1, TNXB, COL4A1, ITGA3, ITGA4, COL5A2, LAMA4, ITGA5, COL1A2,	434	83	5738	3.98	7.20E-07	3.60E-07	5.30E-06				
KEGG_PATHWAY	mmu04610:Complement and coagulation cascades	22	2.03	7.69E-08	PLAT, C7, CSAR1, MASP1, C3, C4B, CFB, F13A1, SERPING1, C1S, C1QC, PLAU, C1Q4, C1Q8, C1RA, THBD, F3, SERPINE1, C3H,	434	75	5738	3.88	1.27E-05	4.23E-06	9.33E-05				
KEGG_PATHWAY	mmu04510:Focal adhesion	37	3.41	4.52E-07	CD9, PROS1, PLAU, MYL2, PGF, TNC, COL3A1, RAC2, COMP, COL6A2, COL6A1, PIK3R5, ZYX, PAK1, COL11A2, THBS1, THBS2, THBS3, FN1, SPP1, THBS4, ACTB, EGFR, COL4A1, TNXB, ACTN1, ITGA3, ITGA4, FNC, BIRC3, FLNB, COL5A2, LAMA4, ITGA5, FYN,	434	198	5738	2.47	7.45E-05	1.86E-05	5.48E-04				
KEGG_PATHWAY	mmu04210:Apoptosis	22	2.03	1.18E-06	MAP3K14	434	87	5738	3.34	1.95E-04	3.89E-05	1.43E-03				
KEGG_PATHWAY	mmu04062:Chemokine signaling pathway	33	3.04	4.28E-06	CXCL1, ADCY4, CCL3, CCL2, GNAI3, CCR1, CXCL2, CCL9, CXCL9, NFKBIA, NFKB1, CXCR2, PFA, GNG11, CCL7, CCL6, CCL24, RAC2, STAT1, PTX2B, CXCR4, PIK3R5, PAK1, LYN, RELA, STAT3,	434	182	5738	2.40	7.05E-04	1.18E-04	5.19E-03				
KEGG_PATHWAY	mmu04010:MAPK signaling pathway	41	3.78	1.37E-05	GADD45B, MAP3K14, GADD45A, CD14, PLAU, C1Q4	434	265	5738	2.05	2.26E-03	3.23E-04	1.66E-02				

Table S2.B KEGG pathways significant at 10 hours

Category	Term	Count	%	PValue	Genes		ListTotal	PopHits	PopTotal	FoldEnrichment	Bonferroni	Benjamini	FDR
KEGG_PATHWAY	mmu00190:Oxidative phosphorylation	80	2.10	8.69e-22	ATP6, UQCRC2, ATP5E, COX11, UQCRC1, COX10, ATP5B, CYC1, NDUFAB1, UQCRCFS1, COXSA, COX5B, UQCRC, NDUF57, NDUF56, NDUF55, UQCRC11, UQCRC1, NDUF58, ATP5L, ATP50, NDUF53, ATP5H, NDUF51, ATP5K, ATP5S, COX15, NDUFB10, NDUF2, COX42, COX41, ATP6V1H, NDUF1, NDUF10, COX6, NDUF11, ATP6V1A, UQCRC, ATP5C1, UQCRC8, NDUF33, NDUF48, NDUF85, NDUF6, NDUF87, NDUF89, COX7B, COX7C, ATP6V1B2, ATP5G1, COX7A2L, ATP5G3, NDUF2, COX6B1, NDUF4, NDUF44, NDUF45, NDUF42, ATP52, COX7A2, NDUF3, NDUF48, COX11, COX8B, NDUF49, NDUF46, NDUF47, ATP5F1, NDUF41, PP2A, SDHA, NDUFV3, SDH6,	1276	130	5738	2.77	1.64E-19	1.64E-19	1.08E-18	
KEGG_PATHWAY	mmu05012:Parkinson's disease	80	2.10	6.54e-21	ATP6V2, UQCRC2, ATP5E, NDUFV2, SDH6, ATP5A1 NDUF5D, UQCRC2, ATP5E, SMCAP, UQCRC1, ATP5B, UBE2G1, CYC1, SNC4, NDUFAB1, UQCRCFS1, COXSA, COX5B, UQCRC, NDUF57, NDUF56, NDUF55, CAP3, UQCRC10, UQCRC11, NDUF58, ATP50, NDUF53, ATP5H, NDUF51, ATP5K, NDUFB10, NDUF2, COX42, COX41, ATP6V1H, NDUF1, NDUF10, COX6, NDUF11, ATP6V1A, UQCRC, ATP5C1, UQCRC8, NDUF33, NDUF48, NDUF85, NDUF6, NDUF87, NDUF89, COX7B, COX7C, ATP5G1, COX7A2L, ATP5G3, NDUF2, POLR2A, ITAM, COX6B1, TMG2, PRP3, NDUF44, NDUF45, NDUF42, COX7A2, NDUF3, NDUF48, COX7A1, COX8B, HTT, NDUF49, DNAL1C1, NDUF46, CREBBP, NDUF47, ATP5F1, VDAC3, NDUF41, SOD2, NDUFV3, SDHA, SDHB, SP1, BBC3, NDUFV1, SDHC, BAX, NDUFV2, SDHD, ATPA1, ATP5A1	1276	133	5738	2.70	1.24E-18	6.18E-19	8.12E-18	
KEGG_PATHWAY	mmu05016:Huntington's disease	95	2.49	1.19e-18	ATP5D, UQCRC2, ATP5E, UQCRC1, ATP5B, SNCA, CYC1, NDUFAB1, REST, CLTC, COXSA, UQCRCFS1, COX5B, UQCRC, NDUF57, GPIX, NDUF56, NDUF55, NDUF54, NDUF53, UQCRC10, UQCRC11, NDUF58, PLCB4, CASP8, NDUF88, CRESB2, ATP50, NDUF53, ATP5H, NDUF51, ATP5K, NDUFB10, NDUF2, COX42, COX41, ATP6V1H, NDUF1, NDUF10, COX6, NDUF11, ATP6V1A, COX6C, UQCRC, ATP5C1, UQCRC8, NDUF33, NDUF48, NDUF85, NDUF6, NDUF87, NDUF89, COX7B, COX7C, ATP5G1, COX7A2L, ATP5G3, NDUF2, POLR2A, ITAM, COX6B1, TMG2, PRP3, NDUF44, NDUF45, NDUF42, COX7A2, NDUF3, NDUF48, COX7A1, COX8B, HTT, NDUF49, DNAL1C1, NDUF46, CREBBP, NDUF47, ATP5F1, VDAC3, NDUF41, SOD2, NDUFV3, SDHA, SDHB, SP1, BBC3, NDUFV1, SDHC, BAX, NDUFV2, SDHD, ATPA1, ATP5A1	1276	183	5738	2.33	2.24E-16	7.48E-17	1.47E-15	
KEGG_PATHWAY	mmu05010:Alzheimer's disease	93	2.44	1.09e-17	ATP5D, UQCRC2, ATP5E, UQCRC1, ATP5B, SNCA, CYC1, NDUFAB1, UQCRCFS1, COXSA, COX5B, UQCRC, NDUF57, NDUF56, NDUF55, CAP3, UQCRC10, UQCRC11, NDUF58, ATP50, FA, NDUF53, ATP5H, NDUF51, ATP5K, NDUFB10, ADAM10, CYCS, NDUF2, COX42, COX41, ATP6V1H, NDUF1, NDUF10, COX6, COX6C, UQCRC, BACE1, ATP5C1, Eif2AK3, UQCRC, BBL, NDUF33, NDUF48, NDUF85, CDK5R1, NDUF2, NDUF87, NDUF89, COX7B, COX7C, ATP5G1, COX7A2L, ATP5G3, NDUF2, POLR2A, ITAM, COX6B1, TMG2, PRP3, NDUF44, NDUF45, NDUF42, COX7A2, NDUF3, NDUF48, COX7A1, COX8B, HTT, NDUF49, DNAL1C1, NDUF46, CREBBP, NDUF47, ATP5F1, VDAC3, NDUF41, SOD2, NDUFV3, SDHA, SDHB, SP1, BBC3, NDUFV1, SDHC, BAX, COX7A1, COX8B, NDUF49, NDUF46, NDUF47, ATP5F1, CAP2N, NDUF41, ATP2R, AT6F, SDHA, NDUFV3, SDH6, ATP5D, ATPA1, ATP2A2, ATP2A3, NDUFV1, SDHC, NDUFV2, CAP2Z, SDHA, ATPA1, ATP5A1, CALM2 PBDGA, PGDFA, NDUF49, NDUF46, NDUF47, ATP5F1, CHAD, VCL, ACTG1, ARHGPAS, PAK2, PAK3, SHC1, ZYX, COL1A2, COL1A1L, PRKCA, EGR, PARVG, ACTN4, BRAF, ROCK1, ROCK2, ACTN2, ACTN2, FLCN, PDGFRA, LAMC2, LAMC1, COL1A1, VASP, VEGFB, CCND1, CCND2, JUN, VEGFA, COL1A2, PDGFRA, LAMC2, LAMC1, COL1A1, CAV3, IBSP, MYL2, TNC, COL3A1, COL2A1, ITGB1, PKN, MYL9, IFGFR, DOK1, LAMB2, RAC2, COMP, ITGB7, ITGB6, COL6A2, PPPIR12A, COL6A1, PIK3R5, THBS1, THBS2, PIK3R1, THBS3, FN1, THBS4, SP1, PIK3R2, ACTB, COL4A2, COL4A4, PLT1, TNXB, MET, BIRC3, CAPN2, COL5A2, VAV1, KDR, VWF, LAMA4, TGAs, G0R1, RAP1B, DIA1	1276	182	5738	2.30	2.07E-15	5.17E-16	1.36E-14	
KEGG_PATHWAY	mmu04510:Focal adhesion	82	2.15	1.46e-09	AT5C, ALC2, SUCLG1, C3, IDH8, ACY, DLAT, OGDH, PDHB, IDH3A, SDHA, SDHB, IDH3G, SDHC, DLD, SDH6, IDH2, IDH1, PDHA1, FHL1, SUCL2, HADH, MHD2, MHD1 UQCRC2, ATP1B1, QCRC1, MYL2, ATP1B3, TNNC1, MYL3, ATP1B4, CYC1, UQCRC7, COX7C, CACN81, COX7A2L, QCRCFS1, COXSA, COX5B, UQCRC, TPM4, TPM3, UQCRC10, COX6B1, ACTC1, SLC8A1, QCRC2, COX8B, COX7A1, COX42, COX41, MYH7, ATP1A1, COX6C, CACNA2D4, ATP2A2, COL6A2, COL6A1, AGRN, COL1A2, THBS1, COL1A1, THBS2, THBS3, FN1, SPP1, THBS4, COL4A2, COL4A1, TNXB, COL5A2, VWF, LAMA4, SDC1, C036, TGAs, COL1A2, LAMC2, LAMC1, COL1A1 BCAT2, EHADH, ACAT1, ACAT1, HADHA, HIBADH, AHDH, HADH, MHC2, MTC, MUC6, OCTX1, MHC1, ACAD8, HADH, HMGC, BCKDH, AACAD, ACAD8, DABT, DLD, ATP1A1, HXB1, CIRH, PCCA FGD7, PDKB, PGDFA, TGF8, NFKB2, TGF1B1, PRK2, TGF2B, PRK2, MYC, CHUK, MAP2K2, PRK2, ERFA, BRAF, RELB, PTPR, ECST, FLCN, FLNB, STK3, MAP4K3, MAP4K4, RASGRF2, ARRB2, RAS2, JUN, GADD45G, PGDFA, HSPI1, MAPK7, MAPK14, GADD45A, IL1R1, IL1R1, FGR3, MNKN2, DUSP10, MAP4K2, CACN81, HSP1A1, GNG12, HSP1A1, TNFSF11, KRS, HSP2A, RASGRP3, RAC2, ELK4, MAP2K2, PLAK2G12A, JUND, RASGRF2, HSP48, RAS42, PTPN7, TRP3, TGFBR1, TGFBR2, NR4A1, MAPK11, TBL1, ACNA2D4, PRPSK6A5, DUSP, NRAS, DUSP4, ATP4, PLAK2G4A, RPSK6A3, DUSP2, RPSK6A4, DUSP1, RPSK6A2, NTRK2, RAP1B, PLA2G4B, CD14, DUSP7 ITGAL, GNAI3, MYL2, GNAI1, MMP9, BCAR1, CLDN5, ITGB2, MMP2, TGFBI, SLC2A1, RBL, CSFR, RARA, FAS, RARB, EGFR, RET, BCR, BRAF, RELA, RNRK, CTNNA1, VEGF, JUP, HIF1A, JUN, VEGFA, PGDFA, LAMC2, LAMC1, WNTSA, GFRP3, SFP1, BCL2L1, ITGB1, KRS, LAMB2, RAC2, F1H, RUNX1, AXIN2, CSF1R, FN1, AXIN2, TRP3, BMP2, TCF7, PDE4B, EPAS1, TGFBR1, MET, CREBBP, TGFBR2, SMAD3, CBLB, LAMK, CDK11A, PLCG2, PRAR, FGF, NFKB2, FOS, CNE1, CAP39, CAP58, FG2, MYC, CSF2RA, CHUK, PRKA, AR, HSP90AA1, CYCS, CDK4, SMO, CCND1, MDM2, WNT11, WNT9A, BID, PML, KIT, TPF3, IGF1R, PIK3R5, CEBPA, IL6, COL4A2, COA41, MSH2, FZD1, BIRC3, FZD5, STAT3, RALGDS, NRAS, HSP90AA1, RASSF5, BAX, RASSF1, JAK1	1276	198	5738	1.86	2.76E-07	5.53E-08	1.82E-06	
KEGG_PATHWAY	mmu00020:Citrate cycle (TCA cycle)	23	0.60	8.98e-09	SDH6, IDH2, IDH1, PDHA1, FHL1, SUCL2, HADH, MHD2, MHD1 UQCRC2, ATP1B1, QCRC1, MYL2, ATP1B3, TNNC1, MYL3, ATP1B4, CYC1, UQCRC7, COX7C, CACN81, COX7A2L, QCRCFS1, COXSA, COX5B, UQCRC, TPM4, TPM3, UQCRC10, COX6B1, ACTC1, SLC8A1, QCRC2, COX8B, COX7A1, COX42, COX41, MYH7, ATP1A1, COX6C, CACNA2D4, ATP2A2, COL6A2, COL6A1, AGRN, COL1A2, THBS1, COL1A1, THBS2, THBS3, FN1, SPP1, THBS4, COL4A2, COL4A1, TNXB, COL5A2, VWF, LAMA4, SDC1, C036, TGAs, COL1A2, LAMC2, LAMC1, COL1A1 BCAT2, EHADH, ACAT1, ACAT1, HADHA, HIBADH, AHDH, HADH, MHC2, MTC, MUC6, OCTX1, MHC1, ACAD8, HADH, HMGC, BCKDH, AACAD, ACAD8, DABT, DLD, ATP1A1, HXB1, CIRH, PCCA FGD7, PDKB, PGDFA, TGF8, NFKB2, TGF1B1, PRK2, TGF2B, PRK2, MYC, CHUK, MAP2K2, PRK2, ERFA, BRAF, RELB, PTPR, ECST, FLCN, FLNB, STK3, MAP4K3, MAP4K4, RASGRF2, ARRB2, RAS2, JUN, GADD45G, PGDFA, HSPI1, MAPK7, MAPK14, GADD45A, IL1R1, IL1R1, FGR3, MNKN2, DUSP10, MAP4K2, CACN81, HSP1A1, GNG12, HSP1A1, TNFSF11, KRS, HSP2A, RASGRP3, RAC2, ELK4, MAP2K2, PLAK2G12A, JUND, RASGRF2, HSP48, RAS42, PTPN7, TRP3, TGFBR1, TGFBR2, NR4A1, MAPK11, TBL1, ACNA2D4, PRPSK6A5, DUSP, NRAS, DUSP4, ATP4, PLAK2G4A, RPSK6A3, DUSP2, RPSK6A4, DUSP1, RPSK6A2, NTRK2, RAP1B, PLA2G4B, CD14, DUSP7 ITGAL, GNAI3, MYL2, GNAI1, MMP9, BCAR1, CLDN5, ITGB2, MMP2, TGFBI, SLC2A1, RBL, CSFR, RARA, FAS, RARB, EGFR, RET, BCR, BRAF, RELA, RNRK, CTNNA1, VEGF, JUP, HIF1A, JUN, VEGFA, PGDFA, LAMC2, LAMC1, WNTSA, GFRP3, SFP1, BCL2L1, ITGB1, KRS, LAMB2, RAC2, F1H, RUNX1, AXIN2, CSF1R, FN1, AXIN2, TRP3, BMP2, TCF7, PDE4B, EPAS1, TGFBR1, MET, CREBBP, TGFBR2, SMAD3, CBLB, LAMK, CDK11A, PLCG2, PRAR, FGF, NFKB2, FOS, CNE1, CAP39, CAP58, FG2, MYC, CSF2RA, CHUK, PRKA, AR, HSP90AA1, CYCS, CDK4, SMO, CCND1, MDM2, WNT11, WNT9A, BID, PML, KIT, TPF3, IGF1R, PIK3R5, CEBPA, IL6, COL4A2, COA41, MSH2, FZD1, BIRC3, FZD5, STAT3, RALGDS, NRAS, HSP90AA1, RASSF5, BAX, RASSF1, JAK1	1276	31	5738	3.34	1.70E-06	2.83E-07	1.11E-05	
KEGG_PATHWAY	mmu04260:Cardiac muscle contraction	37	0.97	2.11e-06	IBSP, TNC, NPNT, COL3A1, COL2A1, SDC4, ITGB1, SDC2, CHAD, LAMB2, CD44, COMP, ITGB7, ITGB6, COL6A2, COL6A1, AGRN, COL1A2, THBS1, COL1A1, THBS2, THBS3, FN1, SPP1, THBS4, COL4A2, COL4A1, TNXB, COL5A2, VWF, LAMA4, SDC1, C036, TGAs, COL1A2, LAMC2, LAMC1, COL1A1 BCAT2, EHADH, ACAT1, ACAT1, HADHA, HIBADH, AHDH, HADH, MHC2, MTC, MUC6, OCTX1, MHC1, ACAD8, HADH, HMGC, BCKDH, AACAD, ACAD8, DABT, DLD, ATP1A1, HXB1, CIRH, PCCA FGD7, PDKB, PGDFA, TGF8, NFKB2, TGF1B1, PRK2, TGF2B, PRK2, MYC, CHUK, MAP2K2, PRK2, ERFA, BRAF, RELB, PTPR, ECST, FLCN, FLNB, STK3, MAP4K3, MAP4K4, RASGRF2, ARRB2, RAS2, JUN, GADD45G, PGDFA, HSPI1, MAPK7, MAPK14, GADD45A, IL1R1, IL1R1, FGR3, MNKN2, DUSP10, MAP4K2, CACN81, HSP1A1, GNG12, HSP1A1, TNFSF11, KRS, HSP2A, RASGRP3, RAC2, ELK4, MAP2K2, PLAK2G12A, JUND, RASGRF2, HSP48, RAS42, PTPN7, TRP3, TGFBR1, TGFBR2, NR4A1, MAPK11, TBL1, ACNA2D4, PRPSK6A5, DUSP, NRAS, DUSP4, ATP4, PLAK2G4A, RPSK6A3, DUSP2, RPSK6A4, DUSP1, RPSK6A2, NTRK2, RAP1B, PLA2G4B, CD14, DUSP7 ITGAL, GNAI3, MYL2, GNAI1, MMP9, BCAR1, CLDN5, ITGB2, MMP2, TGFBI, SLC2A1, RBL, CSFR, RARA, FAS, RARB, EGFR, RET, BCR, BRAF, RELA, RNRK, CTNNA1, VEGF, JUP, HIF1A, JUN, VEGFA, PGDFA, LAMC2, LAMC1, WNTSA, GFRP3, SFP1, BCL2L1, ITGB1, KRS, LAMB2, RAC2, F1H, RUNX1, AXIN2, CSF1R, FN1, AXIN2, TRP3, BMP2, TCF7, PDE4B, EPAS1, TGFBR1, MET, CREBBP, TGFBR2, SMAD3, CBLB, LAMK, CDK11A, PLCG2, PRAR, FGF, NFKB2, FOS, CNE1, CAP39, CAP58, FG2, MYC, CSF2RA, CHUK, PRKA, AR, HSP90AA1, CYCS, CDK4, SMO, CCND1, MDM2, WNT11, WNT9A, BID, PML, KIT, TPF3, IGF1R, PIK3R5, CEBPA, IL6, COL4A2, COA41, MSH2, FZD1, BIRC3, FZD5, STAT3, RALGDS, NRAS, HSP90AA1, RASSF5, BAX, RASSF1, JAK1	1276	78	5738	2.13	3.99E-04	5.70E-05	0.002622723	
KEGG_PATHWAY	mmu04512:ECM-receptor interaction	38	1.00	4.27e-06	SDH6, IDH2, IDH1, PDHA1, FHL1, SUCL2, HADH, MHD2, MHD1 UQCRC2, ATP1B1, QCRC1, MYL2, ATP1B3, TNNC1, MYL3, ATP1B4, CYC1, UQCRC7, COX7C, CACN81, COX7A2L, QCRCFS1, COXSA, COX5B, UQCRC, TPM4, TPM3, UQCRC10, COX6B1, ACTC1, SLC8A1, QCRC2, COX8B, COX7A1, COX42, COX41, MYH7, ATP1A1, COX6C, CACNA2D4, ATP2A2, COL6A2, COL6A1, AGRN, COL1A2, THBS1, COL1A1, THBS2, THBS3, FN1, SPP1, THBS4, COL4A2, COL4A1, TNXB, COL5A2, VWF, LAMA4, SDC1, C036, TGAs, COL1A2, LAMC2, LAMC1, COL1A1 BCAT2, EHADH, ACAT1, ACAT1, HADHA, HIBADH, AHDH, HADH, MHC2, MTC, MUC6, OCTX1, MHC1, ACAD8, HADH, HMGC, BCKDH, AACAD, ACAD8, DABT, DLD, ATP1A1, HXB1, CIRH, PCCA FGD7, PDKB, PGDFA, TGF8, NFKB2, TGF1B1, PRK2, TGF2B, PRK2, MYC, CHUK, MAP2K2, PRK2, ERFA, BRAF, RELB, PTPR, ECST, FLCN, FLNB, STK3, MAP4K3, MAP4K4, RASGRF2, ARRB2, RAS2, JUN, GADD45G, PGDFA, HSPI1, MAPK7, MAPK14, GADD45A, IL1R1, IL1R1, FGR3, MNKN2, DUSP10, MAP4K2, CACN81, HSP1A1, GNG12, HSP1A1, TNFSF11, KRS, HSP2A, RASGRP3, RAC2, ELK4, MAP2K2, PLAK2G12A, JUND, RASGRF2, HSP48, RAS42, PTPN7, TRP3, TGFBR1, TGFBR2, NR4A1, MAPK11, TBL1, ACNA2D4, PRPSK6A5, DUSP, NRAS, DUSP4, ATP4, PLAK2G4A, RPSK6A3, DUSP2, RPSK6A4, DUSP1, RPSK6A2, NTRK2, RAP1B, PLA2G4B, CD14, DUSP7 ITGAL, GNAI3, MYL2, GNAI1, MMP9, BCAR1, CLDN5, ITGB2, MMP2, TGFBI, SLC2A1, RBL, CSFR, RARA, FAS, RARB, EGFR, RET, BCR, BRAF, RELA, RNRK, CTNNA1, VEGF, JUP, HIF1A, JUN, VEGFA, PGDFA, LAMC2, LAMC1, WNTSA, GFRP3, SFP1, BCL2L1, ITGB1, KRS, LAMB2, RAC2, F1H, RUNX1, AXIN2, CSF1R, FN1, AXIN2, TRP3, BMP2, TCF7, PDE4B, EPAS1, TGFBR1, MET, CREBBP, TGFBR2, SMAD3, CBLB, LAMK, CDK11A, PLCG2, PRAR, FGF, NFKB2, FOS, CNE1, CAP39, CAP58, FG2, MYC, CSF2RA, CHUK, PRKA, AR, HSP90AA1, CYCS, CDK4, SMO, CCND1, MDM2, WNT11, WNT9A, BID, PML, KIT, TPF3, IGF1R, PIK3R5, CEBPA, IL6, COL4A2, COA41, MSH2, FZD1, BIRC3, FZD5, STAT3, RALGDS, NRAS, HSP90AA1, RASSF5, BAX, RASSF1, JAK1	1276	83	5738	2.06	8.06E-04	1.01E-04	0.005297508	
KEGG_PATHWAY	mmu000280:Valine, leucine and isoleucine degradation	25	0.66	7.94e-06	SDH6, IDH2, IDH1, PDHA1, FHL1, SUCL2, HADH, MHD2, MHD1 UQCRC2, ATP1B1, QCRC1, MYL2, ATP1B3, TNNC1, MYL3, ATP1B4, CYC1, UQCRC7, COX7C, CACN81, COX7A2L, QCRCFS1, COXSA, COX5B, UQCRC, TPM4, TPM3, UQCRC10, COX6B1, ACTC1, SLC8A1, QCRC2, COX8B, COX7A1, COX42, COX41, MYH7, ATP1A1, COX6C, CACNA2D4, ATP2A2, COL6A2, COL6A1, AGRN, COL1A2, THBS1, COL1A1, THBS2, THBS3, FN1, SPP1, THBS4, COL4A2, COL4A1, TNXB, COL5A2, VWF, LAMA4, SDC1, C036, TGAs, COL1A2, LAMC2, LAMC1, COL1A1 BCAT2, EHADH, ACAT1, ACAT1, HADHA, HIBADH, AHDH, HADH, MHC2, MTC, MUC6, OCTX1, MHC1, ACAD8, HADH, HMGC, BCKDH, AACAD, ACAD8, DABT, DLD, ATP1A1, HXB1, CIRH, PCCA FGD7, PDKB, PGDFA, HSPI1, MAPK7, MAPK14, GADD45A, IL1R1, IL1R1, FGR3, MNKN2, DUSP10, MAP4K2, CACN81, HSP1A1, GNG12, HSP1A1, TNFSF11, KRS, HSP2A, RASGRP3, RAC2, ELK4, MAP2K2, PLAK2G12A, JUND, RASGRF2, HSP48, RAS42, PTPN7, TRP3, TGFBR1, TGFBR2, NR4A1, MAPK11, TBL1, ACNA2D4, PRPSK6A5, DUSP, NRAS, DUSP4, ATP4, PLAK2G4A, RPSK6A3, DUSP2, RPSK6A4, DUSP1, RPSK6A2, NTRK2, RAP1B, PLA2G4B, CD14, DUSP7 ITGAL, GNAI3, MYL2, GNAI1, MMP9, BCAR1, CLDN5, ITGB2, MMP2, TGFBI, SLC2A1, RBL, CSFR, RARA, FAS, RARB, EGFR, RET, BCR, BRAF, RELA, RNRK, CTNNA1, VEGF, JUP, HIF1A, JUN, VEGFA, PGDFA, LAMC2, LAMC1, WNTSA, GFRP3, SFP1, BCL2L1, ITGB1, KRS, LAMB2, RAC2, F1H, RUNX1, AXIN2, CSF1R, FN1, AXIN2, TRP3, BMP2, TCF7, PDE4B, EPAS1, TGFBR1, MET, CREBBP, TGFBR2, SMAD3, CBLB, LAMK, CDK11A, PLCG2, PRAR, FGF, NFKB2, FOS, CNE1, CAP39, CAP58, FG2, MYC, CSF2RA, CHUK, PRKA, AR, HSP90AA1, CYCS, CDK4, SMO, CCND1, MDM2, WNT11, WNT9A, BID, PML, KIT, TPF3, IGF1R, PIK3R5, CEBPA, IL6, COL4A2, COA41, MSH2, FZD1, BIRC3, FZD5, STAT3, RALGDS, NRAS, HSP90AA1, RASSF5, BAX, RASSF1, JAK1	1276	46	5738	2.44	0.001499078	1.67E-04	0.009856236	
KEGG_PATHWAY	mmu04010:MAPK signaling pathway	90	2.36	9.02e-06	ATP6, UQCRC2, ATP5E, COX11, UQCRC1, COX10, ATP5B, CYC1, NDUFAB1, UQCRCFS1, COXSA, COX5B, UQCRC, NDUF57, NDUF56, NDUF55, UQCRC10, UQCRC11, NDUF58, ATP5L, ATP50, NDUF53, ATP5H, NDUF51, ATP5K, ATP5S, COX15, NDUFB10, NDUF2, COX42, COX41, ATP6V1H, NDUF1, NDUF10, COX6, NDUF11, ATP6V1A, UQCRC, ATP5C1, UQCRC8, NDUF33, NDUF48, NDUF85, ATP5G1, COX7A2L, ATP5G3, NDUF2, POLR2A, ITAM, COX6B1, TMG2, PRP3, NDUF44, NDUF45, NDUF42, COX7A2, NDUF3, NDUF48, COX7A1, COX8B, HTT, NDUF49, DNAL1C1, NDUF46, CREBBP, NDUF47, ATP5F1, VDAC3, NDUF41, SOD2, NDUFV3, SDHA, SDHB, SP1, BBC3, NDUFV1, SDHC, BAX, NDUFV2, SDHD, ATPA1, ATP5A1	1276	265	5738	1.53	0.001703641	1.70E-04	0.011202286	
KEGG_PATHWAY	mmu04670:Leukocyte transendothelial migration	47	1.23	3.16e-05	IBSP, CYB, CBB, RASSF5, PLCG2, GFRF1, PLA2G8, TAK1, JAK2, ACTG1, ARHGPAS, EZR, PAK2, PTK28, MIP1, RAS2, PTPN7, TRP3, TGFBR1, GFRF2, TGFBR2, SMAD2, CBLB, LAMK, CDK11A, PLCG2, PRAR, FGF, NFKB2, FOS, CNE1, CAP39, CAP58, FG2, MYC, CSF2RA, CHUK, PRKA, AR, HSP90AA1, CYCS, CDK4, SMO, CCND1, MDM2, WNT11, WNT9A, BID, PML, KIT, TPF3, IGF1R, PIK3R5, CEBPA, IL6, COL4A2, COA41, MSH2, FZD1, BIRC3, FZD5, STAT3, RALGDS, NRAS, HSP90AA1, RASSF5, BAX, RASSF1, JAK1	1276	119	5738	1.78	0.005957607	5.43E-04	0.039252835	
KEGG PATHWAY	mmu050200:Pathways in cancer	103	2.70	3.93e-05	STAT3, RALGDS, NRAS, HSP90AA1, RASSF5, BAX, RASSF1, JAK1	1276	323	5738	1.43	0.007403353	6.19E-04	0.04881099	

Table S2.C KEGG pathways significant at 24 hours

Table S2.D KEGG pathways significant at 48 hours

Table S2.E KEGG pathways significant at 72 hours

KEGG_PATHWAY	mmu05212:Pancreatic cancer	47	0.65	9.20E-06	E2F1, E2F2, PGF, NFKB1, BCL2L1, TGF β 1, TGF β 2, AKT1, ACRV1B, RAC2, CASP9, RAC3, RALB, RALA, PIK3CA, PIK3RS, EGF, FIGF, AKT3, AKT2, PIK3CG, TRP53, EGFR, PDL1, RELA, ARHGEEF6, TGF β R1, PIK3CD, TGF β R2, SMAD4, RAF1, BRC2, SMAD3, CDK6, STAT1, CDK4, STAT3, RALGDS, RAD51, VEGF, CCND1, ARAF, VEGFA, MAPK3, MAPK9, MAPK8, IKBKB, TGF β 1, TGF β 2, AKT1, FOS, ACRV1B, CASP3, CASP9, PIK3CA, MYC, AKT3, AKT2, EGFR, PIK3CG, PIK3CD, CYCS, CCND1, JUN, MAPK3, PDGFRA, MAPK9, MAPK8, GRB2, TCF7L2, RAC2, RAC3, SOS1, BCL2, SOS2, PIK3RS, DVL2, FZD9, TRP53, TCF7, MSH3, MSH2, TGF β R2, SMAD4, FZD1, RAF1, SMAD3, BIRC5, FZD2, FZD5, APPBP1, FZD4, FZD7, RALGDS, FZD6, DVL1, BAX, GSK3B, ARAF, E2F1, E2F2, GRB2, STAT5B, NFKBIA, NFKB1, BCL2L1, TGF β 1, TGF β 2, AKT1, ACRV1B, GAB2, SOS1, SOS2, PIK3CA, SHC1, PIK3RS, RUNX1, MYC, AKT3, AKT2, PIK3C, TRP53, CTBP1, ICR, MAP2K2, RELA, TGF β R1, CBL, PIK3CD, TGF β R2, SMAD4, RAF1, SMAD3, CDK6, MECOM, CDK4, PTPN11, HRAS1, NRAS1	2203	72	5738	1.70	0.001774079	9.86E-05	0.011463648
KEGG_PATHWAY	mmu05210:Colorectal cancer	53	0.73	2.43E-05	BIRC5, FZD2, FZD5, APPBP1, FZD4, FZD7, RALGDS, FZD6, DVL1, BAX, GSK3B, ARAF, E2F1, E2F2, GRB2, STAT5B, NFKBIA, NFKB1, BCL2L1, TGF β 1, TGF β 2, AKT1, ACRV1B, GAB2, SOS1, SOS2, PIK3CA, SHC1, PIK3RS, RUNX1, MYC, AKT3, AKT2, PIK3C, TRP53, CTBP1, ICR, MAP2K2, RELA, TGF β R1, CBL, PIK3CD, TGF β R2, SMAD4, RAF1, SMAD3, CDK6, MECOM, CDK4, PTPN11, HRAS1, NRAS1	2203	86	5738	1.61	0.004670485	2.46E-04	0.030220506
KEGG_PATHWAY	mmu05220:Chronic myeloid leukemia	48	0.67	2.60E-05	CCND1, CDKN1A, HDAC2, HDAC1, ARAF, MAPK3, MDM2, IKBKB	2203	76	5738	1.65	0.005013764	2.51E-04	0.032446929

Table S2.F KEGG pathways significant at 168 hours

Category	Term	Count	% PValue	Genes							
					List Total	Pop Hits	Pop Total	Fold Enrichment	Bonferroni	Benjamini	FDR
KEGG_PATHWAY	mmu04062:Chemokine signaling pathway	18	0.65 4.47E-07	PIK3R5, XCL1, XCR1 CCL2, FGR, NCF1, HCK, CCL9, WAS, CCL7, CCL17, PRKCB, CCL12, CCR5, RAC2, CCR2, CX3CR1,	129	182	5738	4.40	4.78E-05	4.78E-05	5.02E-04
KEGG_PATHWAY	mmu04670:Leukocyte transendothelial migration	14	0.50 1.93E-06	NCF2, NCF1, NCF4, ITGB2, PRKCB, VCAM1, CYBA, CYBB, EZR, RAC2, PLCG2, CLDN2, PIK3R5, RHOH	129	119	5738	5.23	2.06E-04	1.03E-04	0.002168346
KEGG_PATHWAY	mmu04650:Natural killer cell mediated cytotoxicity	13	0.47 1.46E-05	BID, FCGR4, ITGB2, NCR1, PRKCB, FCGR3, CD48, RAC2, PLCG2, FCER1G, PIK3R5, LCP2, TYROBP	129	122	5738	4.74	0.001563801	5.22E-04	0.016439609
KEGG_PATHWAY	mmu05322:Systemic lupus erythematosus	12	0.43 1.55E-05	C1Q _A , C1Q _B , C7, CD86, C4B, FCGR4, H2-DMB1, HIST1H4I, C1Q _C , FCGR1, IL10, FCGR3 CCL2, CSF2RB2, CCL9, CCL8, IL10, CCL7, CCL17, CCL12, CCR5, IL10RA, CCR2, CX3CR1, CSF2RB, IL2RG,	129	103	5738	5.18	0.001652768	4.13E-04	0.017375573
KEGG_PATHWAY	mmu04060:Cytokine-cytokine receptor interaction	18	0.65 2.48E-05	IL12B, XCL1, XCR1, CSF2RA IL12B, XCL1, XCR1	129	244	5738	3.28	0.00265068	5.31E-04	0.027879105

Table S2.G KEGG pathways significant at 336 hours

Category	Term	Count	%	PValue	Genes	List	Total	Pop	Hits	Pop	Total	Fold	Enrichment	Bonferroni	Benjamini	FDR
KEGG_PATHWAY	mmu04512:ECM-receptor interaction	18	2.36	7.85E-08	COL1A1, THBS2, THBS3, SPP1, FN1, IBSP, TNC, COL3A1, ITGB5, ITGA4, COL5A3, COL5A2, SDC2, COL5A1, CD44, COL1A2, COL6A2, COL6A1, H2-K1, TGAL, MYH3, H2-D1, H2-DMB1, ITGB2, MYH7, H2-AB1, MYH8, CD86, H2-EB1, SGCD, H2-AA, PARD3, CCL2, ADCY7, NCF1, STAT5B, CXCL9, CCL9, CCL8, GNG11, PF4, CCL6, CCL12, CCR5, ADCY9, PARD3, CCL2, ADCY7, NCF1, STAT5B, CXCL9, CCL9, CCL8, GNG11, PF4, CCL6, CCL12, CCR5, ADCY9, IBSP, FLT1, TNC, COL3A1, ITGB5, ITGA4, COL5A3, COL5A2, COL5A1, GSK3B, BCL2, SOS2, COL6A2, IBSP, FLT1, TNC, COL3A1, ITGB5, ITGA4, COL5A3, COL5A2, COL5A1, GSK3B, BCL2, SOS2, COL6A2, GRLF1, COL1A2, COL6A1, COL1A1, PAK1, EGF, SHC2, THBS2, THBS3, SPP1, FN1	254	83	5738	4.90	1.08E-05	1.08E-05	9.24E-05				
KEGG_PATHWAY	mmu05416:Viral myocarditis	16	2.10	1.24E-05	MYH13, MYH14, ABL2	254	94	5738	3.85	0.001713391	8.57E-04	0.014623985				
KEGG_PATHWAY	mmu04062:Chemokine signalling pathway	23	3.01	1.34E-05	TIAM1, CXCR4, GNG10, CXCL16, GSK3B, CCR2, SOS2, PAK1, SHC2	254	182	5738	2.85	0.001841954	6.14E-04	0.015722211				
KEGG_PATHWAY	mmu04510:Focal adhesion	24	3.15	1.64E-05	GRLF1, COL1A2, COL6A1, COL1A1, PAK1, EGF, SHC2, THBS2, THBS3, SPP1, FN1	254	198	5738	2.74	0.002258263	5.65E-04	0.019279342				

Table S2.H KEGG pathways significant at 504 hours

Category	Term	Count	%	Pvalue	Genes
KEGG_PATHWAY	mmu04512:ECM-receptor interaction	18	2.36	7.85E-08	IBSP, TNC, COL3A1, ITGB5, ITGA4, COL5A3, COL5A2, SDC2, COL5A1, CD44, COL1A2, COL6A2, COL6A1
KEGG_PATHWAY	mmu05416:Viral myocarditis	16	2.10	1.24E-05	MYH3, MYH1, MYH4, ABL2
KEGG_PATHWAY	mmu04062:Chemokine signaling pathway	23	3.01	1.34E-05	TIAM1, CXCR4, GNGL10, CXCL16, GSK3B, CCR2, SOS2, PAK1, SHC2
KEGG_PATHWAY	mmu04510:focal adhesion	24	3.15	1.64E-05	GRIP1, COL1A2, COL6A1, COL1A1, PAK1, EGF, SHC2, ITGB2, COL5A2, COL5A3, GSK3B, BCL2, SOS2, COL6A2, THBS2, THBS3, SP1, FN1

Table S2.H KEGG pathways significant at 504 hours

List Total	Pop Hits	Pop Total	Fold Enrichment	Bonferroni	Benjamini	FDR
254	83	5738	4.90	1.08E-05	1.08E-05	9.24E-05
254	94	5738	3.85	0.001713391	8.57E-04	0.014623985
254	182	5738	2.85	0.001841954	6.14E-04	0.015722211
254	198	5738	2.74	0.002258263	5.65E-04	0.019279342

Table S2.1 KEGG pathways significant at 672 hours

Category	Term	Count	%	PValue	Genes	List Total	Pop Hits	Pop Total	Fold Enrichment	Bonferroni	Benjamini	FDR
KEGG_PATHWAY	mmu04512:ECM-receptor interaction	17	2.51	7.58E-08	IBSP, TNC, COL3A1, ITGA4, COL5A2, SDC2, COL5A1, CD44, COMP, COL1A2, COL6A2, COL6A1, COL1A1, THBS2, COL1A1, THBS3, FN1	223	83	5738	5.27	1.08E-05	1.08E-05	8.96E-05
KEGG_PATHWAY	mmu04510:Focal adhesion	26	3.85	1.21E-07	IBSP, CAV2, CAV1, MYL2, TNC, COL3A1, BCL2, COMP, COL6A2, COL6A1, PAK1, EGF, COL11A1, THBS2, FN1, VAV3, IGF1, ITGA4, COL5A1, PDGFRA, COL1A2, GRF1, COL1A1, PARVA	223	198	5738	3.38	1.72E-05	8.62E-06	1.44E-04
KEGG_PATHWAY	mmu04610:Complement and coagulation cascades	15	2.22	7.70E-07	C3AR1, CFB, F13A1, SERPING1, C1S, C1QC, C1QH, C1RA, CD55, F3, CFH, C2, CFD, PROS1	223	75	5738	5.15	1.09E-04	3.64E-05	9.10E-04

Table S3. Significant GO clusters identified from the 168h time point that were obtained from differentially expressed genes that were determined to contribute the largest variance at that time point.

Cluster 1: Enrichment Score: 11.54					
Annotation	GO Term	Gene Count	P-value	FDR	
GOTERM_BP_FAT	vasculature development	85	5.20E-14	9.70E-11	
GOTERM_BP_FAT	blood vessel development	83	1.00E-13	1.90E-10	
GOTERM_BP_FAT	blood vessel morphogenesis	69	4.30E-12	8.00E-09	
GOTERM_BP_FAT	angiogenesis	48	3.00E-09	5.60E-06	
Cluster 2: Enrichment Score: 11.31					
Annotation	GO Term	Gene Count	P-value	FDR	
GOTERM_CC_FAT	extracellular matrix	100	2.50E-14	3.60E-11	
SP_PIR_KEYWORD	extracellular matrix	76	7.40E-14	1.10E-10	
GOTERM_CC_FAT	proteinaceous extracellular m	96	9.40E-14	1.40E-10	
GOTERM_CC_FAT	extracellular region part	179	1.10E-09	1.60E-06	
GOTERM_CC_FAT	extracellular matrix part	37	1.50E-08	2.20E-05	
Cluster 3: Enrichment Score: 9.38					
Annotation	GO Term	Gene Count	P-value	FDR	
KEGG_PATHWAY	lysosome	53	2.40E-12	3.00E-09	
SP_PIR_KEYWORD	lysosome	52	5.60E-10	8.30E-07	
GOTERM_CC_FAT	lysosome	60	1.00E-09	1.50E-06	
GOTERM_CC_FAT	lytic vacuole	60	1.30E-09	1.90E-06	
GOTERM_CC_FAT	vacuole	64	6.80E-09	9.90E-06	
Cluster 4: Enrichment Score: 7.85					
Annotation	GO Term	Gene Count	P-value	FDR	
GOTERM_BP_FAT	vesicle-mediated transport	121	2.70E-10	5.00E-07	
GOTERM_BP_FAT	membrane invagination	61	2.10E-09	3.90E-06	
GOTERM_BP_FAT	endocytosis	61	2.10E-09	3.90E-06	
GOTERM_BP_FAT	membrane organization	76	3.10E-08	5.70E-05	
SP_PIR_KEYWORD	endocytosis	31	1.60E-05	2.40E-02	
Cluster 5: Enrichment Score: 7.18					
Annotation	GO Term	Gene Count	P-value	FDR	
GOTERM_BP_FAT	actin filament-based process	61	1.10E-10	2.00E-07	
GOTERM_BP_FAT	actin cytoskeleton organization	57	5.60E-10	1.00E-06	
GOTERM_BP_FAT	actin filament organization	23	6.70E-06	1.20E-02	
GOTERM_BP_FAT	cytoskeleton organization	76	4.80E-05	8.80E-02	